

Investigating differences in dynamic stability and physiological impairments in persons with multiple sclerosis based on fall history

BY

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## **Abstract**

Around 60% of persons with multiple sclerosis (MS) experience falls, however the cause of these falls is not well understood. The purpose of this study is to further our understanding of why persons with MS fall during gait. Falls most frequently occur during walking, and are most commonly attributed to loss of balance and tripping. While fall occurrence is high, not all persons with MS fall, suggesting that there may be underlying differences between fallers and non-fallers with MS. Only three studies to date have compared walking between persons with MS with a history of falls and persons with MS with no falls history, and these studies have only measured walking speed and spatiotemporal parameters. The first goal of this study is, therefore, to compare specific features of dynamic balance between persons with MS who have a history of falls, persons with MS who have no falls history, and healthy controls. Also, while persons with MS can develop many different physiological impairments, it is unknown which specific physiological impairments are altered in fallers with MS relative to non-fallers and are associated with gait instability. The second goal of this study is, therefore, to determine if physiological impairments are different between persons with MS with a history of falls and persons with MS with no fall history, and to examine the relationship between physiological impairments and dynamic balance in persons with MS. By understanding of why persons with MS fall, these results may lead to improved methods of predicting and preventing falls.

Fifty-five persons with MS (27 recurrent fallers, 28 non-fallers) and twenty-seven healthy controls walked on a treadmill for 3 minutes at their self-selected pace. Physiological impairments (sensorimotor delays, spasticity, plantar cutaneous sensation, and the sensory, cerebellar, and pyramidal Expanded Disability Status Scale subscales) were examined in all

persons with MS. Variability of trunk accelerations, margin of stability, minimum toe clearance during swing phase, and spatiotemporal parameters during the walking trial were compared between all three groups. Physiological impairments were compared between fallers and non-fallers with MS. The relationship between physiological impairments and dynamic balance in persons with MS was assessed using correlation coefficients. Compared to non-fallers and healthy controls, fallers with MS walked more cautiously, with decreased control of the center of mass, and with lower toe clearance during swing phase. Fallers also had more severe physiological impairments than non-fallers. Worse physiological impairment was associated with worse dynamic balance in persons with MS.

The present work provides evidence that within a group of persons with MS, there are specific measurable differences in dynamic balance and physiological impairments that are influenced by falls history which likely help to explain why some individuals with MS fall. It was found that fallers with MS have poor control over their center of mass and lower toe clearances during swing phase relative to non-fallers and healthy controls, which seems to be compensated for by adapting to a slow cautious gait. As dynamic balance was associated with loss of sensory information, longer sensorimotor delays, and pyramidal motor impairments, instability appears to be multifactorial in persons with MS. Evaluating distinct dynamic balance and physiological impairments in persons with MS may provide useful indicators of disease progression and fall risk, lead to improved fall prevention strategies, and aid in evaluating an individual's responsiveness to different interventions.

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### **List of Abbreviations**

MS	Multiple Sclerosis
PwMS	Persons with Multiple Sclerosis
AP	Anterior-posterior
ML	Mediolateral
MoS	Margin of Stability
CoM	Center of Mass
BoS	Base of Support
MTC	Minimum Toe Clearance
LyE	Lyapunov Exponents
SaEn	Sample Entropy
RMS	Root Mean Square
EDSS	Kurtzke's expanded disability status scale
FA	Fallers
NF	Non-Fallers
HC	Healthy controls

## **Chapter 1: Introduction and motivation**

The purpose of this project is to identify if dynamic balance and physiological impairments are different between persons with multiple sclerosis (PwMS) who have a history of falls, PwMS who do not have a falls history, and healthy controls. Specific biomechanical and physiological measures that are altered in PwMS who fall relative to those who do not fall and healthy controls may help explain why many PwMS experience falls. These measured differences may serve as useful indicators of disease progression and fall risk in PwMS.

Approximately 500,000 persons in the United States and 2.1 million people worldwide have MS [1]. MS causes demyelination of axons in the central nervous system, resulting in many physiological impairments which negatively affect gait and balance. Up to 60% of PwMS experience falls [2-6], which often result in injuries, high healthcare costs, and activity curtailment [1, 3-6]. Though fall occurrence is high, not all PwMS fall. Falls most commonly occur during functional mobility, and are most commonly attributed to loss of balance and tripping [6-8]. It is possible that non-fallers and fallers have adapted to the physiological impairments caused by MS differently [9-11], however it is also possible that fallers have worse motor control compared to non-fallers which results in balance dysfunction and falls [12, 13]. While extensive research has found that PwMS walk more cautiously than healthy controls [9, 14-17] and with increased amounts of variability reflecting poor motor control and balance [17-21], to our knowledge only three studies have compared gait between fallers and non-fallers with MS [10, 11, 13]. Furthermore, these studies have investigated only walking speed and spatiotemporal parameters (ie step length and width) which does not explain how the center of mass is controlled [10, 11, 13]. As falls are commonly attributed to loss of balance [7, 8], and

stability is defined as maintaining the center of mass inside the base of support [22], it is important to investigate if fallers and non-fallers control their center of mass differently. PwMS also report trip-related falls [6, 8], however measures reflecting the probability of tripping [23, 24] have not been evaluated in this population. Axonal demyelination can slow or block neural conduction, which depending on the location and nature of the demyelination can result in symptoms including numbness in distal extremities, vision problems, muscle weakness, fatigue, spasticity, and cognitive changes [25]. Extensive research has examined the contributions of physiological impairments to static balance [26-29], but falls most frequently occur during dynamic activities, such as walking [6-8]. Static and dynamic balance are controlled through different mechanisms and have been found to be unrelated [30, 31]. It is currently not well understood which physiological impairments are altered in fallers relative to non-fallers or which impairments are associated with dynamic instability.

Due to the progressive nature and unpredictable disease course of MS, it is important to track how gait and balance change with time in order to understand how the disease is progressing and to what extent balance is impaired to predict and prevent falls. Understanding specific features of dynamic balance and physiological impairments altered in fallers with MS relative to non-fallers may lead to improved methods of identifying individuals at risk for falls and selecting appropriate individualized strategies to reduce fall risk. Additionally, by targeting and evaluating specific features of dynamic balance and physiological impairment through intervention programs, fall prevention strategies may be improved and intervention responsiveness may be sensitively quantified.

## **Chapter 2: Background and Significance**

### **2.1 Epidemiology and consequence of multiple sclerosis**

Approximately 500,000 people in the United States and 2.1 million worldwide have multiple sclerosis (MS), a disease where the body's immune cells target and attack oligodendrocytes and myelin causing inflammation and damage to myelin and axons [25, 32, 33]. Axonal demyelination typically starts to form around medium blood vessels in the optic nerves, periventricular white matter, cerebellum, brain stem, and spinal cord [25]. MS is progressive and unpredictable with demyelination throughout the central nervous system. MS is most commonly diagnosed between the ages of 20 and 50 [1, 32], and while the cause of MS is unknown, specific genetic and environmental factors may predispose individuals to develop the disease [25, 32]. The prevalence of MS is highest in Europe, Australia, and North America. Certain factors have been associated with MS prevalence, such as smoking and vitamin D exposure [25, 32]. Females are 2-3 times more likely to be diagnosed with MS than males [25, 32].

As the central nervous system is the control center for the entire body, MS results in many different physiological symptoms [25, 32]. Typical symptoms of MS include gait and balance impairment, sensory disturbances (numbness and vision), fatigue/decreased energy, cognitive impairment, emotional changes, pain, bladder and bowel dysfunction, and sexual dysfunction [25, 32]. These symptoms lead to employment troubles, depression issues, hospital admittances, and decreased social function, which results in an increased cost of living and a decreased health-related quality of life [1, 34]. Gait and balance impairments result from many different physiological impairments [11], and result in a higher risk for falls in PwMS. Between

50 and 60% of PwMS will fall in a 3 to 6 month period [2, 4-6, 11, 35]. Falls often result in injuries requiring medical attention such as bone fractures, soft tissue damage (bruises or sprains), and head injuries [5, 6, 8]. Falls also commonly lead to fear of falling which can lead to activity curtailment and muscular deconditioning [3]. PwMS most commonly fall during dynamic activities such as walking and transfer [6-8], and are most commonly attributed to loss of balance or tripping [6-8].

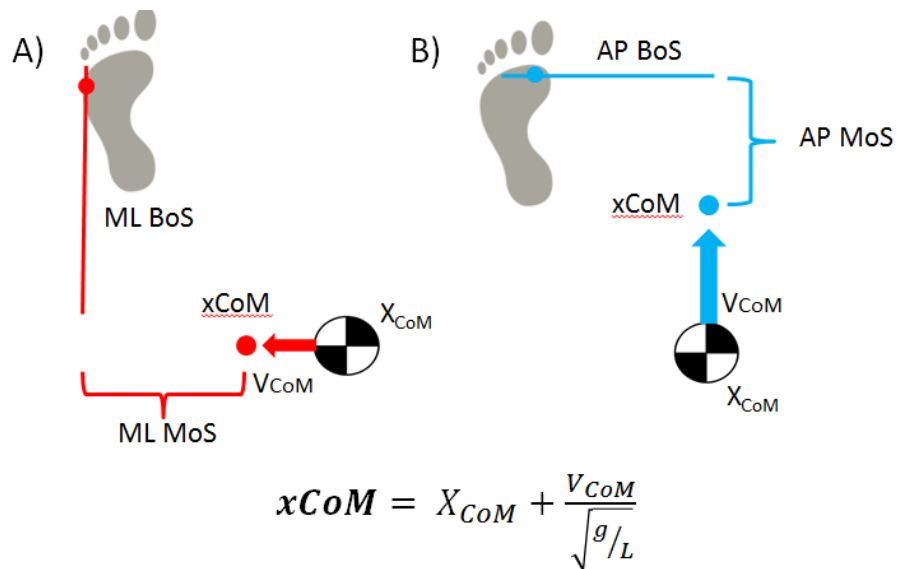
## **2.2 Mobility and balance impairment in multiple sclerosis**

Multiple sclerosis is a progressive and unpredictable disease that impairs gait and balance and leads to a high risk for falling. PwMS have altered lower extremity joint kinematics and kinetics throughout the gait cycle, as well as altered muscular recruitment compared to healthy controls [14-16]. PwMS have increased asymmetry of weight distribution during static balance [36] and during gait [37]. Stance phase asymmetries were found to be predictive of falls in PwMS [10], leading researchers to believe that unilateral strength deficits lead to gait asymmetry and contribute to instability. PwMS also walk slowly, take short and wide steps, and spend more time in double support phase compared to healthy controls [14-17]. These spatiotemporal (step length, width, and time) differences can be observed in minimally impaired PwMS [14], and progressively change with disease progression [38]. Furthermore, fallers with MS walk slower [11] and with a wider base of support (BoS) [10] than non-fallers. While these spatiotemporal differences may be due to muscular weakness [39], evidence shows that they also reflect an adopted cautious gait strategy to preserve stability [9] and are indicative of 'fear of falling' rather than 'risk of falling' [40]. However, stride-to-stride variability of spatiotemporal measures reflects the consistency of the timing and placement of steps is

able to prospectively identify elderly individuals at risk for falling [40, 41]. PwMS have increased amounts of spatiotemporal variability compared to healthy controls [17, 19, 42], and evidence exists relating spatiotemporal variability to fall risk in PwMS [12, 13].

While spatiotemporal measures reveal important information about the BoS during gait, these measures don't incorporate how the CoM is controlled. As gait is a dynamic task, the position of the CoM alone does not accurately portray its kinematic state, and the velocity needs to be accounted for in the 'extrapolated CoM' (Figure 1) [22, 43, 44]. The distance between the extrapolated CoM and the edge of the BoS is referred to as the Margin of Stability (MoS) [22, 43, 44], and can be quantified in the anterior-posterior (AP) or mediolateral (ML) direction at any instant in time [9, 45]. A positive MoS means that the CoM is stable inside the BoS, whereas a negative MoS means the CoM has left the BoS [45]. In the AP direction, MoS is constantly transitioning from positive to negative as the CoM proceeds beyond the stance foot BoS, which is stabilized with the next step being placed anteriorly restoring a positive MoS [9]. In the ML direction, MoS remains positive throughout the gait cycle, and a negative MoS needs to be corrected in the following steps to avoid falling [45]. MoS is generally larger when walking with slow and wide steps [9, 46, 47] with PwMS and other fall risk populations maintaining similar or larger MoS compared to healthy controls, speculated to reflect a cautious gait adaption [9, 40, 44, 48-50]. However, our recent work showed that increased AP and ML MoS at heel strike in PwMS positively correlated with the self-reported number of falls in the previous six months, revealing that this cautious gait adaptation is unhealthy [9]. These gait adaptations are speculated to allow for more response time to external perturbation [9, 40], to account for excessive and irregular trunk motions [9, 20, 49], or to account for less precise

control of step placement [44, 51, 52]. MoS is maintained and adjusted through step placements [44, 53], which can be shown by examining the relationship between CoM motion and step placement [54-56]. Deviations in the position and velocity of the CoM during swing phase are corrected by adjusting the location of the following step, which gives rise to the ‘constant margin’ hypothesis stating that humans aim to maintain a consistent MoS to remain stable [53]. Stride-to-stride variability is therefore argued to reflect dynamic balance better than average MoS during gait as it quantifies how regular step placements are relative to CoM motions and may predict the likelihood of the CoM leaving the BoS [45, 48, 57]. While MoS variability has never been quantified in PwMS, persons recovering from a stroke [48], who have a prosthetic leg [44], and elderly individuals [58] have all been shown to have increased MoS variability compared to healthy controls, which may give rise to an increased risk of falling.



**Figure 1:** Visual representation of the margin of stability (MoS) calculation in the A) Mediolateral (ML) and B) Anterior-Posterior (AP) direction. The extrapolated center of mass (xCoM) incorporates the position ( $X_{CoM}$ ) and velocity ( $V_{CoM}$ ) of the center of mass, the acceleration of gravity ( $g$ ), and leg length ( $L$ ). MoS is then calculated as the distance between the extrapolated center of mass and the edge of the base of support (BoS).



While MoS evaluates the interaction between the CoM and BoS, dynamic balance can be evaluated by investigating the magnitude and structure of motion of upper body segments alone [20, 59-62]. The trunk (torso) is an important body segment to control during gait as it supports the head, which houses vital sensory organs [63], and reflects the motion of the CoM [64]. Root mean square (RMS) transformations are commonly applied to both center of pressure time series [65] as well as cyclical gait time series [20], and is a measure of the dispersion of the measurement relative to zero [66]. Compared to healthy controls, both stroke patients [67] and PwMS [20] have lower trunk acceleration RMS during gait, essentially revealing that these populations have lower magnitude of accelerations. While linear variability measures such as RMS describe the dispersion of a time series, nonlinear variability measures, such as Lyapunov Exponents (LyE) and Sample Entropy (SaEn) quantify the predictability and complexity of a time series. Gait is complex as it involves the interaction of many functional physiological components to produce and control movement [68]. Multiple sclerosis impairs many of these functional components and the coupling between them, which in turn changes the predictability and adaptability of gait [20, 21]. LyE evaluate the ability of an individual to attenuate small ‘local perturbations’ or mechanical disturbances and neuromuscular control errors to maintain functional locomotion during unperturbed gait [69, 70], and are defined as “the average exponential rates of divergence or convergence of nearby orbits of an attractor in phase space” [71, 72]. LyE are predictive of the ability to successfully respond to larger external perturbations in experimental settings and computational models of gait [59, 73], and are able to differentiate elderly fallers from non-fallers [60, 61]. PwMS have larger LyE of trunk motions than healthy controls, which could be related to an increased likelihood of losing control over

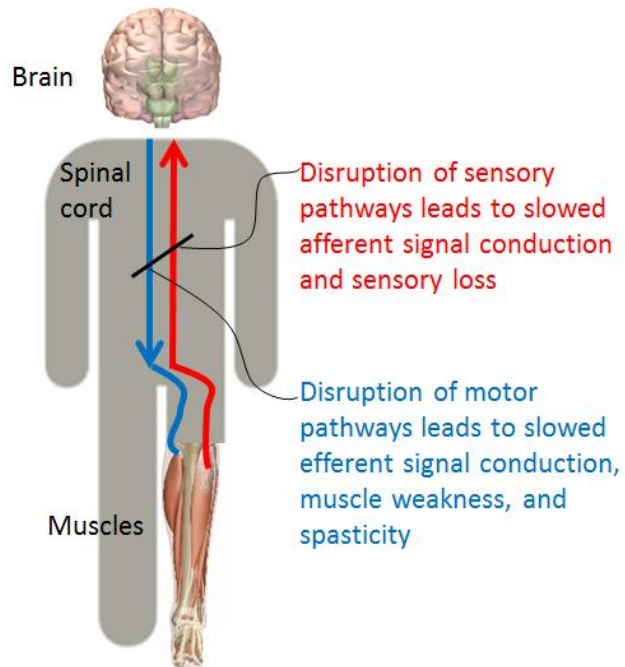
the center of mass during gait [20]. Entropy can be defined as “the loss of information in a signal”, and is often used to assess the periodicity or regularity in human movement [74]. Entropy has been used extensively to study the predictability of biological signals including heart rate dynamics [75], red blood cell dynamics [76], postural control [77], step placements during gait [21, 74], and trunk motions during gait [20, 61, 78]. Compared to healthy controls, PwMS have lower entropy in their step lengths and step widths, which represents more predictable and less adaptable stepping strategy [21].

A common external perturbation experienced during gait is a trip, where the swing foot contacts the ground (or obstacle on the ground) and transforms the body’s linear momentum to angular velocity as the CoM falls [79, 80]. Though PwMS often report tripping as a fall attribute [6, 8], to our knowledge, features of foot control during swing phase of gait in PwMS has not been previously evaluated. During level ground gait, a trip is most likely to occur at the time of minimum toe clearance (MTC) where the toe reaches its minimum distance from the ground. Compared to young adults elderly individuals have been found to walk with a similar or higher average MTC during gait [81], however they have an increased variability in sequential MTC [23, 81-83] which reflects a swing foot control deficit which may contribute to their risk of tripping. Since PwMS experience trip related falls [6], as well as increased variability of lower limb joint angles during stance and swing [19], it is likely that there are changes in the foot clearance during swing phase that is related to increased risk of experiencing a trip.

### **2.3 Physiological impairments in multiple sclerosis**

The hallmark disease feature of MS is demyelination of axons throughout the central nervous system. As myelin insulates and protects these axons, signals sent along demyelinated

axons can be slowed down, distorted, or blocked all together (Figure 2) [25, 33]. Slowed neural conduction can be experimentally quantified by measuring the time it takes for somatosensory evoked potentials to propagate up the spinal cord [84], or for a muscle to activate following stimulation of the primary motor cortex [85]. Slowed neural conduction speed can also be observed when measuring response time to external perturbations, which is commonly done by translating a support surface and measuring the time lapse between the onset of translation and the onset of muscular activity [84]. This time lapse will be referred to here as sensorimotor delays as perturbation responses rely on both afferent and efferent pathways. Sensorimotor delays are longer in PwMS compared to controls, and correlate with conduction speed of somatosensory evoked potentials up the spinal cord [84]. Sensorimotor delays are functionally important as they are correlated with postural instability during quiet stance and altered trunk motions during gait [27]. Long sensorimotor delays likely reduce the ability of PwMS to quickly receive and integrate sensory information regarding the state of the CoM during swing phase and modify muscular activity to adapt step placement, thus contributing to poor dynamic balance.



**Figure 2:** Visual representation of the origin of sensory and motor impairments in persons with multiple sclerosis

One of the first symptoms of MS is sensory loss, which is often described as impaired or blurred vision or numbness/tingling in the distal extremities [32]. PwMS typically do not have complete loss of function of sensory systems, however the quality of sensory feedback is commonly degraded. Cutaneous receptors in the sole of the foot are believed to play a dominant role in maintaining balance [86]. Cutaneous receptors are distributed throughout the sole of the foot, and are therefore able to ‘map’ the pressure distribution under the foot [86]. PwMS [86], elderly individuals [86], and persons with diabetic peripheral neuropathy [87], who are all at an increased risk for falls, all have loss of sensation at the sole of the foot. Foot cutaneous sensation is commonly and reliably quantified by use of a Vibratron device, in which the amplitude of a vibrating knob is increased and the lowest amplitude accurately identified by the subject is recorded, with lower amplitudes being reflective of more sensation [88].

Vibration thresholds at the feet are correlated with impaired balance during quiet stance and slower gait speeds in PwMS [28, 88, 89].

Motor impairments are also very common symptoms among PwMS, and are characterized by weaker maximum force production, slower rates of force production, increased rates of fatigue development, less control of force development and hyperreflexia [10, 39, 90-92]. Spasticity, defined as an exaggerated velocity-dependent stretch reflex, which is present in over 80% of PwMS and affects activities of daily life [93]. Spasticity is associated with poor static balance and slower walking speeds in PwMS [29], and has been speculated to contribute to increased gait variability by altering the outcome of descending motor commands [42].

## **2.4 Summary**

The purpose of this study is to further our understanding of why PwMS fall during gait. While it is known that fallers with MS walk slower, with wider and more variable steps than non-fallers, specific features of dynamic balance that are different between fallers and non-fallers remains unknown. Gait features such as center of mass control and swing foot height may help explain why some PwMS fall and others remain stable while walking. Distinct physiological impairments such as slowed neural conduction speeds, sensory loss, and spasticity are associated with impaired static balance and slow preferred walking speeds in PwMS, however it is unknown how these impairments relate to dynamic instability and fall risk. Due to the progressive nature and unpredictable disease course of MS, it is important to evaluate how gait and balance change with time in order to understand disease progression and to predict and prevent falls. Gait in PwMS is currently clinically evaluated with tests depicting quantity of

gait, such as walking speed, which doesn't quantify the quality or safety of movement. Through furthering the current understanding of the biomechanical and physiological mechanisms of instability in PwMS this study hopes to lead to improved methods of predicting falls, to improved strategies of preventing falls, and to improved methods of quantifying intervention efficacy.

## **Chapter 3: Dynamic balance in persons with multiple sclerosis who have a falls history is altered compared to non-fallers and to healthy controls**

### **3.1 Abstract**

Around 60% of persons with multiple sclerosis (MS) experience falls, however the dynamic balance differences between those who fall and those who don't are not well understood. The purpose of this study is to identify distinct biomechanical features of dynamic balance during gait that are different between fallers with MS, non-fallers with MS, and healthy controls. 27 recurrent fallers with MS, 28 persons with MS with no falls history, and 27 healthy controls walked on a treadmill at their preferred speed for 3 minutes. The variability of trunk accelerations and the average and variability of minimum toe clearance, spatiotemporal parameters, and margin of stability were compared between groups. Fallers with MS exhibited a slower cautious gait compared to non-fallers and healthy controls, but had decreased anterior-posterior margin of stability and minimum toe clearance. Fallers walked with less locally stable and predictable trunk accelerations, and increased variability of step length, stride time, and both anterior-posterior and mediolateral margin of stability compared to non-fallers and healthy controls. The present work provides evidence that within a group of persons with MS, there are gait differences that are influenced by falls history. These differences indicate that in persons with MS who fall, the center of mass is poorly controlled through base of support placement and the foot is closer to the ground during swing phase relative to the non-fallers. These identified biomechanical differences could be used to evaluate dynamic balance in persons with MS and to help improve fall prevention strategies.

### 3.2 Introduction

Multiple sclerosis (MS) is a progressive disease that causes demyelination and axonal loss in the central nervous system resulting in a variety of sensory and motor impairments which negatively affect gait and balance including spasticity, sensory loss, muscular deconditioning, and decreased neural conduction velocity [25, 27]. Between 50-60% of persons with MS (PwMS) experience falls [3, 5, 6] with over half of falls resulting in injury requiring medical attention [5, 6]. Falls also lead to high healthcare costs, lower health-related quality of life [1], and fear of falling with associated activity curtailment [3]. Falls most commonly occur during functional mobility such as walking [6, 7]. While fall occurrence is high in PwMS, up to 50-60% of individuals [3, 5, 6], not all PwMS fall. Fallers with MS may have made different gait adaptations [9-11] or have different levels of motor control impairment [12, 13] than non-fallers with MS. Although previous research has identified important features of dynamic balance which are altered during gait in PwMS relative to healthy controls [17, 20], it is unclear if these dynamic balance features are associated with falls.

PwMS walk with slower, shorter, and wider steps and spend more time in double-support than healthy controls [17]. However, contradicting evidence exists relating these gait changes to fall risk since it was found that fallers walked slower than non-fallers but with similar step widths [11], and that step width significantly contributed to fall risk but velocity did not [10]. This discrepancy may be due to traditional spatiotemporal measures (e.g. step length, width, and time) of gait being reflective of 'fear of falling' rather than risk of falling [40]. Spatiotemporal variability, however, reveals important features of sensorimotor impairment and has well documented success in prospectively identifying elderly fallers [40, 94]. While



evidence exists linking increased spatiotemporal variability to falls in PwMS [12, 13], experimental design limitations hinder the generalizability of the results. Some studies have looked at gait variability only over a short distance (7.9 m) [13], which may lead to unreliable results [95], while others compared variability to a physiological fall risk assessment rather than actual fall occurrence [12]. No studies have specifically compared dynamic balance between fallers and non-fallers with MS.

Dynamic balance, or gait stability, has been quantified in many different ways [70]. Nonlinear variability measures have been used to quantify the predictability and complexity of dynamic systems which is reflective of gait stability [70]. For example, Lyapunov exponent is predictive of the ability to successfully respond to larger external perturbations [59] and of future falls in elderly individuals [60]. PwMS have altered nonlinear variability of both spatiotemporal parameters and trunk accelerations during gait [20, 21]. Gait stability may also be defined as the ability to maintain the extrapolated (velocity-adjusted) center of mass (CoM) within the base of support, with the distance between the two referred to as the margin of stability (MoS) [22]. PwMS tend to increase MoS during gait, highlighting a cautious gait adaptation [9]. Increased MoS was positively correlated with self-reported number of falls in PwMS which indicates that the cautious gait adaptation may actually cause instability [9]. While average MoS across strides depicts overall gait strategy (walking slow or taking wide steps), stride-to-stride variability of MoS may be better suited for investigating dynamic balance as it reflects the consistency of step placement relative to CoM motion [45].

While previous research has identified indicators of fall risk in PwMS [10-13], the specific features of gait which contribute to this increased risk are unclear. The purpose of this

study is to identify distinct features of dynamic balance during gait that are different between PwMS who have a history of falls, PwMS with no history of falls, and healthy controls. Previous research has focused only on spatiotemporal footfall information as it related to fall risk [10-13]. As falls in PwMS are most commonly attributed to loss of balance and tripping [6, 7], the present study investigates features of gait which could contribute to balance-related fall risk and trip-related fall risk. Our first hypothesis is that compared to non-fallers and healthy controls, fallers will have a more cautious gait strategy as demonstrated by increased MoS and increased minimum toe clearance (MTC). Previous work has found that fallers with MS walk slower than non-fallers [11], and that slow walking leads to an increased MoS [9] and that elderly fallers had a higher MTC than non-fallers [23]. Elderly fallers are also known to have increased variability of spatiotemporal parameters [40], trunk accelerations [60], and MTC [23]. Therefore, our second hypothesis is that compared to non-fallers and healthy controls, fallers will have increased variability of MoS, MTC, spatiotemporal parameters, and trunk accelerations.

### **3.3 Methods**

#### **3.3.1 Participants**

Twenty-seven healthy controls (HC) and fifty-five PwMS were enrolled in the present study (Table 1). The University of Kansas Medical Center Human Research Committee approved this study and all participants gave informed written consent. HC were free of any known neurological or musculoskeletal pathologies or disorders that would have an adverse effect on the participant's balance or gait. All MS subjects were between the ages of 21-60, had relapsing

remitting MS, and had an EDSS score less than 5.5. The self-reported number of falls in the six months prior to data collection was recorded for PwMS and HC. Non-fallers (NF) were classified as PwMS who did not experience a fall in the previous 6 months (n=28) and fallers (FA) were classified as PwMS with 2 or more falls in the previous 6 months (n=27), as PwMS who fall more than once are more likely to fall due to intrinsic disease specific factors [10]. Demographics were compared between groups using paired t-tests (Table 1).

**Table 1:** Group demographics mean (SD). Independent t-tests compared between groups, with significance set at 0.05. Abbreviations: BMI – Body mass index; 25FTW – timed 25 foot walk; EDSS - Kurtzke’s expanded disability status scale; HC – Healthy Controls; NF – Non-fallers with MS; FA – Recurrent Fallers with MS.

	Group Mean (SD)			Independent t-tests		
	HC (n=27)	NF (n=28)	FA (n=27)	HC-NF	HC-FA	NF-FA
<b>Age</b>	44.96 (9.85)	45.88 (9.48)	46.61 (10.10)	1.000	1.000	1.000
<b>Gender (F/M)</b>	21/6	20/8	19/8	-	-	-
<b>BMI</b>	26.30 (4.03)	27.98 (6.46)	28.56 (8.41)	1.000	0.626	1.000
<b>T25FW (sec)</b>	4.45 (0.61)	4.73 (0.93)	6.33 (1.81)	1.000	<b>&lt;0.001</b>	<b>&lt;0.001</b>
<b>EDSS</b>	-	1.80 (0.93)	2.87 (1.22)	-	-	<b>0.001</b>
<b>Berg Balance Scale</b>	-	54.11 (3.07)	49.63 (7.81)	-	-	<b>0.007</b>
<b>Years since diagnosis</b>	-	10.54 (8.49)	11.67 (8.54)	-	-	0.625
<b>Falls in previous 6 months</b>	0	0	7.78 (12.51)	-	-	<b>0.002</b>
<b>Preferred Walking Speed (m/s)</b>	0.92 (0.31)	0.73 (0.23)	0.51 (0.30)	<b>0.039</b>	<b>&lt;0.001</b>	<b>0.012</b>

### 3.3.2 Data Collection

All subjects walked on a treadmill at their self-selected preferred pace for 3 minutes. Kinematic data was collected at 60 Hz (Motion Analysis, Santa Rosa, CA, USA) using retroreflective markers placed bilaterally on the anterior and posterior superior iliac spine, heel, lateral malleolus, top of the second metatarsal phalangeal joint, and at the lateral metatarsal phalangeal. Wireless inertial sensors (Opal, APDM, Portland, OR, USA) placed on the trunk, over the midline of the sternum, inferior to the manubrium and superior to the xiphoid process was used to measure acceleration at 128 Hz.

### 3.3.3 Data Analysis

#### *Foot motion*

Heel strikes were defined as the anterior-posterior (AP) local maxima of each heel marker's trajectory [96]. Step length and step width were defined as the AP and mediolateral (ML) distance between contralateral heel markers at each left and right step. Stride time was defined as the time between two ipsilateral heel strikes. Spatiotemporal variability was determined using coefficient of variation, which represents the standard deviation normalized by the mean [17].

MTC was defined as the vertical distance from the toe marker to the treadmill, at the local minimum during mid-swing phase [83]. For each true MTC observed, the percent of swing phase was recorded. Occasionally, swing phases occurred which resulted in no true local minimum, and MTC was recorded as the toe height at the average percent of swing phase for other MTC [83]. Participants who exhibited somewhat of a shuffle gait, visually determined as

abnormal swing phases, were excluded for the statistical analysis of MTC only (1 NF; 8 FA). Variability of MTC was determined using the time series standard deviation [23].

### *Trunk acceleration*

Linear accelerations were measured in the AP, ML, and vertical (VT) axis, and analyzed independently. Root mean square transforms (RMS) were used to describe the dispersion of each signal [20, 78]. Temporal structure of trunk accelerations was assessed with Lyapunov exponents (LyE) and sample entropy (SaEn). Raw acceleration time series were down-sampled to 60 Hz and truncated to the middle 60 strides [48, 97]. Delay-embedded state spaces were reconstructed independently in each axis. Embedding dimensions were found using the global false nearest neighbor algorithm, and time delays were found using the average mutual information algorithm [97]. Both algorithms were used on each independent time series, and the median of every subject resulted in an embedding dimension of 7 for each axis, and time delays of 6, 8, and 9 for the AP, ML, and VT axis, respectively [97]. LyE were calculated using Wolf's algorithm. SaEn [98] was calculated with the medium time delays from the average mutual information analysis [78]. Values of  $m=3$  and  $r=0.2$  were used, as these have been found to be robust for SaEn calculations of trunk accelerations [78].

### *Margin of Stability*

Margin of stability was calculated as the distance between the extrapolated CoM and base of support [22], and has been described in detail elsewhere [9]. MoS was calculated in the AP and ML direction at each heel strike [48]. Variability of MoS across the entire 3 minutes was assessed using coefficient of variation [48]. MoS asymmetry was assessed between the left and

right feet using the symmetry index (Equation 1) in the AP and ML direction [99].

$$\text{Symmetry Index} = \frac{|MoS_{right} - MoS_{left}|}{0.5(MoS_{right} + MoS_{left})} \times 100 \quad (1)$$

### 3.3.4 Statistical Comparisons

A one-way anova was used to identify a main effect of Group for each outcome variable. Since RMS is known to be dependent on walking speed [100], walking speed was included as a covariate in the statistical model for this variable. The left and right legs were treated independently for step length, stride time, step width, MTC, and MoS. All extreme outliers were removed prior to statistical comparisons. Post-hoc tests compared between individual groups when a significant effect of Group was found. All statistics were performed with SPSS software (SPSS version 22).

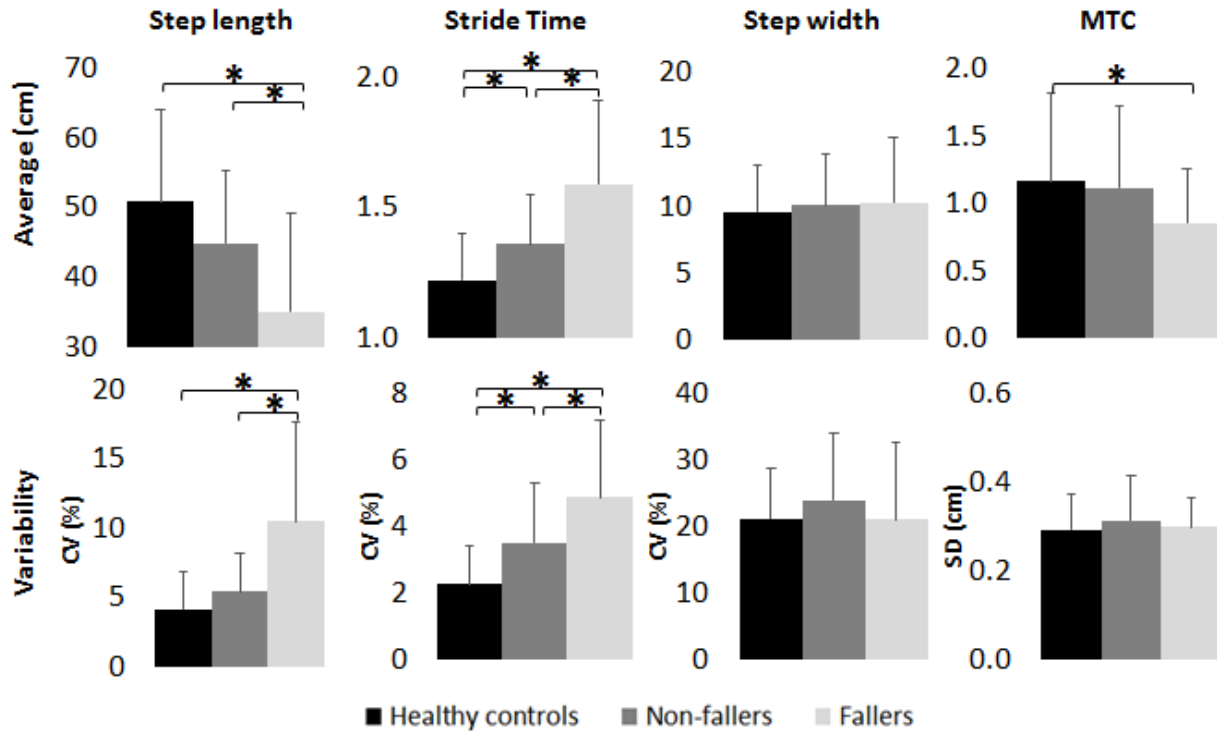
## 3.4 Results

### *Foot Motion*

There was a significant main effect of Group on step length ( $F=21.822$ ,  $p<0.001$ ), stride time ( $F=34.468$ ,  $p<0.001$ ), coefficient of variation of step length ( $F=26.995$ ,  $p<0.001$ ), and coefficient of variation of stride time ( $F=27.515$ ,  $p<0.001$ ) (Table 2; Figure 3). FA walked with significantly shorter steps and slower strides than both HC and NF. FA walked with significantly larger coefficient of variation of step length and stride time than both HC and NF. NF walked significantly slower and with a larger coefficient of variation of stride time than HC. There was a significant main effect of Group ( $F=3.279$ ,  $p=0.041$ ) on MTC where FA had a smaller MTC than HC but no difference in MTC between NF and HC or between NF and FA. Post hoc paired test p-values for all comparisons are found in Table 2.

**Table 2:** Foot motion group mean (SD) for healthy controls (HC), persons with MS who are non-fallers (NF), and persons with MS who are fallers (FA), anova results, and Bonferroni post-hoc comparisons. Due to data collection issues, motion capture data from one FA was excluded, and accelerometer data from one HC was excluded. Abbreviations: CV – coefficient of variation; SD – standard deviation. \*Significant effect,  $p < 0.05$

Outcome Measure	Group Mean (SD)			Effect of Group	Group Pairwise Comparisons		
	HC (n=27)	NF (n=28)	FA (n=27)		HC-NF	HC-FA	NF-FA
AP	Step Length (cm)	50.82 (13.10)	44.84 (10.43)	35.02 (14.27)	<b>F = 21.822</b> <b>(p&lt;0.001)*</b>	0.051	<b>&lt;0.001</b>
	Step Length CV (%)	4.13 (2.77)	5.41 (2.77)	10.47 (7.24)	<b>F = 26.995</b> <b>(p&lt;0.001)*</b>	0.510	<b>&lt;0.001</b>
	Stride Time (sec)	1.22 (0.18)	1.36 (0.19)	1.59 (0.32)	<b>F = 34.468</b> <b>(p&lt;0.001)*</b>	<b>0.006</b>	<b>&lt;0.001</b>
	Stride Time CV (%)	2.26 (1.11)	3.50 (1.77)	4.84 (2.34)	<b>F = 27.515</b> <b>(p&lt;0.001)*</b>	<b>0.001</b>	<b>&lt;0.001</b>
ML	Step Width (cm)	9.56 (3.55)	10.06 (3.77)	10.23 (4.95)	F = 0.527 (p=0.591)		
	Step Width CV (%)	21.07 (7.64)	23.90 (10.05)	20.88 (11.73)	F = 1.205 (p=0.303)		
Vertical	Toe Clearance (cm)	1.16 (0.65)	1.11 (0.61)	0.85 (0.40)	<b>F = 3.279</b> <b>(p=0.041)*</b>	1.000	<b>0.046</b>
	Toe Clearance SD (cm)	0.29 (0.08)	0.31 (0.10)	0.30 (0.06)	F = 0.720 (p=0.488)		0.127



**Figure 3:** Foot motion comparison between healthy controls (HC), persons with MS who are non-fallers (NF), and persons with MS who are fallers (FA). \* represents significant difference between groups ( $p < 0.05$ ). MTC – minimum toe clearance; CV – coefficient of variation; SD – standard deviation.

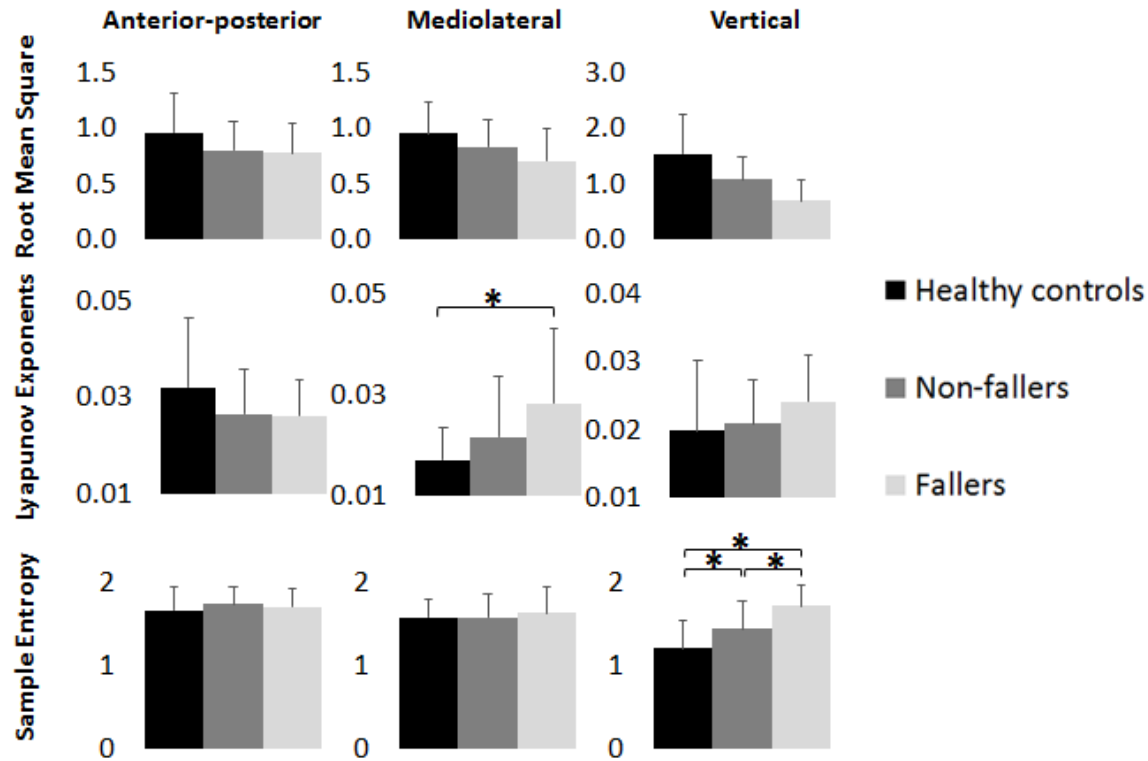
### Trunk Acceleration

There was no effect of Group for RMS. There was a significant main effect of Group ( $F=6.197$ ,  $p=0.003$ ) for LyE where FA had larger LyE compared to HC in the ML direction but not in the AP or VT direction (Table 3; Figure 4). There was a significant effect of Group ( $F=17.101$ ,  $p < 0.001$ ) for SaEn where FA had higher SaEn compared to NF and HC in the VT direction only, and NF had higher SaEn than HC in the VT direction only.



**Table 3:** Trunk accelerations group mean (SD) for healthy controls (HC), persons with MS who are non-fallers (NF), and persons with MS who are fallers (FA), anova results, and Bonferroni post-hoc comparisons. Abbreviations: RMS – root mean square; LyE – Lyapunov exponents; SaEn – sample entropy. \*Significant effect,  $p < 0.05$

	Outcome Measure	Group Mean (SD)			Effect of Group	Group Pairwise Comparisons		
		HC (n=27)	NF (n=28)	FA (n=27)		HC-NF	HC-FA	NF-FA
Dispersion	AP RMS	0.96 (0.36)	0.80 (0.25)	0.77 (0.27)	F=1.802 (p=0.172)			
	ML RMS	0.95 (0.29)	0.83 (0.25)	0.71 (0.30)	F=0.204 (p=0.816)			
	VT RMS	1.54 (0.73)	1.08 (0.40)	0.69 (0.37)	F=1.725 (p=0.185)			
Divergence	AP LyE	0.0321 (0.0144)	0.0265 (0.0095)	0.00262 (0.0075)	F=2.437 (p=0.094)			
	ML LyE	0.0169 (0.0063)	0.0216 (0.0121)	0.0283 (0.0149)	<b>F=6.197</b> <b>(p=0.003)*</b>	0.462	<b>0.002</b>	0.111
	VT LyE	0.0199 (0.0102)	0.0209 (0.0065)	0.0241 (0.0070)	F=2.058 (p=0.135)			
Repeatability	AP SaEn	1.67 (0.29)	1.74 (0.21)	1.71 (0.22)	F=0.675 (p=0.512)			
	ML SaEn	1.58 (0.22)	1.58 (0.28)	1.63 (0.32)	F = 0.329 (p=0.721)			
	VT SaEn	1.21 (0.34)	1.44 (0.34)	1.71 (0.25)	<b>F=17.101</b> <b>(p&lt;0.001)*</b>	<b>0.023</b>	<b>&lt;0.001</b>	<b>0.006</b>



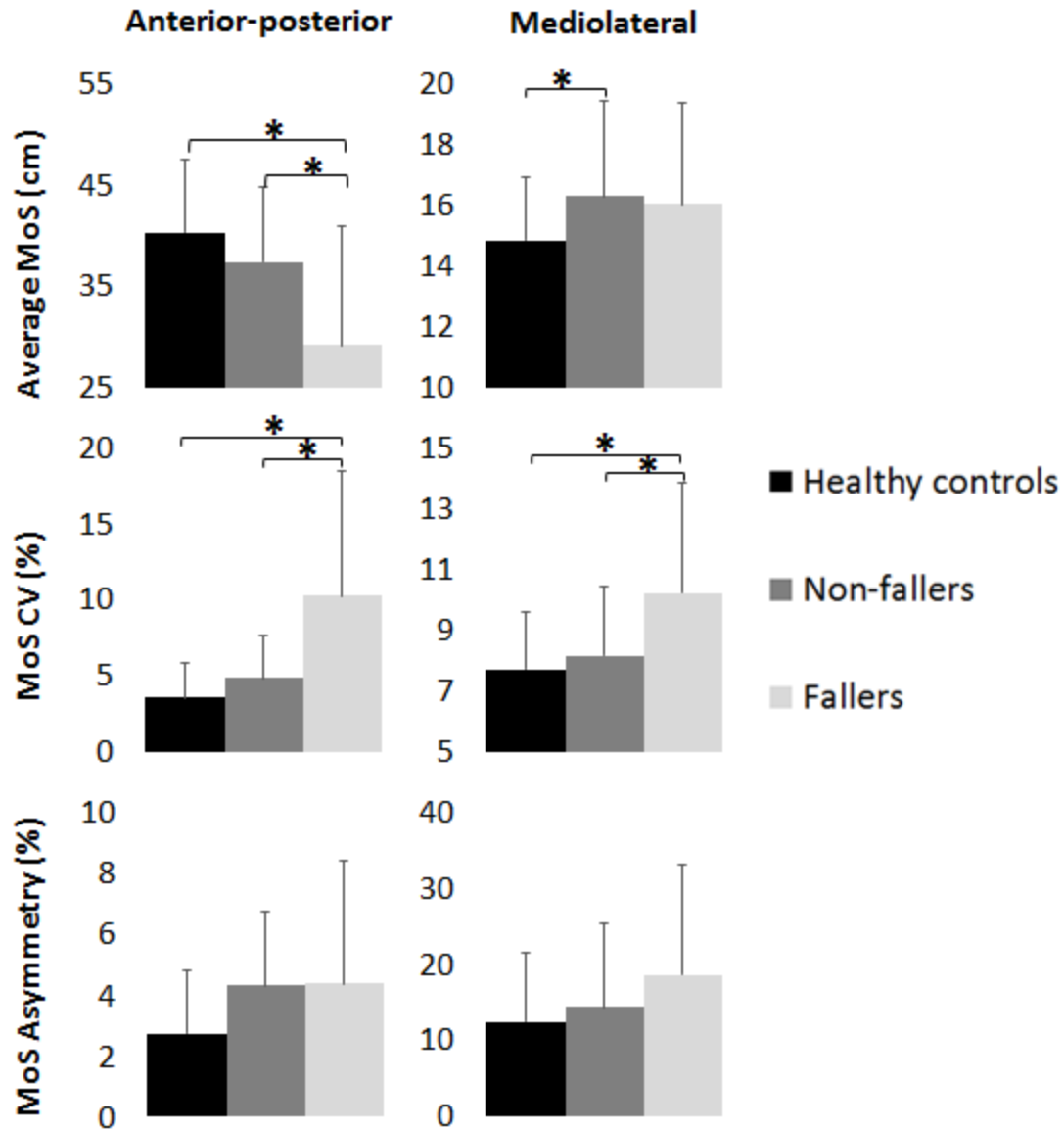
**Figure 4:** trunk accelerations comparison between healthy controls (HC), persons with MS who are non-fallers (NF), and persons with MS who are fallers (FA). \* represents significant difference between groups ( $p < 0.05$ ).

### *Margin of Stability*

There was a significant main effect of Group on mean AP MoS ( $F=21.672$ ,  $p < 0.001$ ) and AP MoS coefficient of variation ( $F=27.700$ ,  $p < 0.001$ ) (Table 4; Figure 5). FA had a decreased mean AP MoS and an increased AP MoS coefficient of variation compared to both NF and HC. There was also a significant main effect of Group on mean ML MoS ( $F=4.602$ ,  $p=0.011$ ) and ML MoS coefficient of variation ( $F=12.692$ ,  $p < 0.001$ ). NF had an increased mean ML MoS compared to HC only, and FA had an increased ML MoS coefficient of variation compared to both NF and HC.

**Table 4:** Margin of Stability (MoS) group mean (SD) for healthy controls (HC), persons with MS who are non-fallers (NF), and persons with MS who are fallers (FA), anova results, and Bonferroni post-hoc comparisons. Abbreviation: CV – coefficient of variation. \*Significant effect,  $p < 0.05$ .

Outcome Measure	Group Mean (SD)			Effect of Group	Group Pairwise Comparisons		
	HC (n=27)	NF (n=28)	FA (n=27)		HC-NF	HC-FA	NF-FA
AP MoS (cm)	40.32 (7.32)	37.45 (7.34)	29.24 (11.82)	<b>F = 21.672</b> <b>(p&lt;0.001)*</b>	0.450	<b>&lt;0.001</b>	<b>&lt;0.001</b>
AP MoS CV (%)	3.63 (2.24)	4.86 (2.90)	10.32 (8.27)	<b>F = 27.700</b> <b>(p&lt;0.001)*</b>	0.742	<b>&lt;0.001</b>	<b>&lt;0.001</b>
AP MoS Asymmetry (%)	2.74 (2.08)	4.32 (2.44)	4.37 (4.08)	F = 2.224 (p=0.116)			
ML MoS (cm)	14.86 (2.11)	16.31 (3.13)	16.04 (3.37)	<b>F = 4.602</b> <b>(p=0.011)*</b>	<b>0.014</b>	0.067	1.000
ML MoS CV (%)	7.73 (1.91)	8.19 (2.29)	10.24 (3.36)	<b>F = 12.692</b> <b>(p&lt;0.001)*</b>	1.000	<b>&lt;0.001</b>	<b>&lt;0.001</b>
ML MoS Asymmetry (%)	12.50 (9.09)	14.37 (11.00)	18.61 (14.62)	F = 2.260 (p=0.111)			



**Figure 5:** Margin of stability (MoS) comparison between healthy controls (HC), persons with MS who are non-fallers (NF), and persons with MS who are fallers (FA). \* represents significant difference between groups ( $p < 0.05$ ). CV – coefficient of variation.

### 3.5 Discussion

The present study identified distinct gait features that are different between PwMS with a history of falls (FA group), PwMS with no fall history (NF group), and healthy controls (HC). These findings are novel and significant as both groups of PwMS were ambulatory with mild-to-moderate disease severity ( $EDSS < 5.5$ ) and had similar ages and years since diagnosis, yet there

were distinct gait parameter differences between these groups which may help explain why some PwMS fall and others remain stable. The first hypothesis, that fallers would have a more cautious gait strategy, was mostly supported since FA walked with shorter and slower steps compared to HC and NF, and both MS groups had a higher ML MoS compared to HC. The next hypothesis, that fallers would have increased gait variability was supported since FA had an increased variability of MoS, step length, and stride time, and altered LyE and SaEn of trunk accelerations compared to NF and HC. These differences may serve as sensitive indicators of balance dysfunction and fall risk in PwMS and could be used to individualize interventions and evaluate intervention responsiveness.

The current results indicate that the FA group had a more cautious gait strategy relative to NF and HC based on slower preferred walking speed, altered spatiotemporal gait characteristics, and altered CoM control. Cautious gait adaptations have been speculated to be a strategy to allow for more response time to external perturbation [9, 40], account for altered trunk motion [9, 20] or for less precise control of step placement [51, 52]. Increasing ML MoS depicts cautious gait well as it quantifies a strategy where the extrapolated CoM is further from the edge of the base of support. We hypothesized that FA would have an increased AP MoS, as previous reports have shown that fallers with MS walk slower than non-fallers [11] and that slower walking increases AP MoS [9]. While FA did walk significantly slower than NF and HC they actually had a decreased AP MoS, indicating that their extrapolated CoM was closer to the anterior limit of their base of support at heel strike. This finding seems to be indicative of an increased likelihood of the CoM leaving the AP base of support in fallers with MS.

The present study found that MTC was lower in FA than HC and MTC variability was

similar between all groups. Lower MTC increases the probability of experiencing a trip during community ambulation, which may lead to a fall [24]. Previous work has shown that elderly fallers have a higher average MTC with more MTC variability compared to non-fallers [23], which suggest different contributing mechanisms to trip-related falls between elderly fallers and fallers with MS.

Step width variability was similar between all groups and mediolateral trunk acceleration variability was similar between FA and NF. Both of these variables are frequently used in literature to quantify lateral balance during gait [20, 60, 101, 102]. Mediolateral MoS variability was, however, significantly higher in FA relative to NF and HC and similar between NF and HC which indicates that the interaction between the CoM and base of support is specifically altered in fallers in the ML direction. Increased MoS variability may increase the likelihood of experiencing a very small or negative MoS in the ML direction at heel strike where the CoM is likely to leave the base of support and a fall would occur [22, 45]. Lateral gait stability requires active control of step placement [101]. Healthy individuals display a significant relationship between CoM motion during swing and subsequent step placement where strides with more lateral CoM motion are met with a more lateral step placement to maintain stability [55, 56]. Post-stroke individuals do not display this relationship between CoM motion and step placement [51], have been found to have a higher ML MoS variability relative to healthy controls [48], and have a very high risk of falls [103]. In PwMS, slowed neural conduction velocity resulting from axonal demyelination is likely the main contributing factor to lateral instability and this slowed conduction velocity may be more severe in the fallers with MS. Slowed neural conduction in PwMS causes a significantly delayed response to postural

perturbations, which is related to static instability and altered trunk motion during gait [27]. These sensorimotor delays may decrease the ability to quickly sense CoM motion during swing phase and adjust step placement. Fall prevention which focuses on restoring healthy step placement [104, 105] and CoM control during various dynamic tasks [106, 107] could be the best strategies to improve dynamic balance in PwMS.

While gait variability in the ML direction is thought to reflect dynamic balance, AP variability is believed to reflect loss of gait rhythmicity [102]. Compared to both NF and HC, FA had significantly increased variability of step length, stride time, and AP MoS. Increased step length variability reflects an inability to make consistent step placements [40] and increased stride time variability is believed to reflect the final output of the locomotor system due to its reliance on both central and peripheral input and feedback to regulate the timing of gait phase transitions [94]. While AP MoS variability has not previously been evaluated in PwMS, our results are similar to post-stroke individuals [48]. LyE and RMS of AP trunk accelerations were similar between groups which is inconsistent with previous results [20] but may be due to the sensitivity of LyE and RMS to walking condition (treadmill verse over-ground) [108] and speed [69]. SaEn of vertical trunk accelerations were different between all three groups, indicating less predictable trunk motions in PwMS compared to HC and in FA compared to NF. Vertical instability is thought be reflective of increased amounts of postural changes or trunk angle changes on a step-by-step basis [109]. Together, these results show that the FA group has a decreased ability to maintain consistent and controlled motions of upper and lower body segments, which are most likely related to specific physiological impairments found in PwMS.

A limitation of our experimental procedure was use of a treadmill for data collection,

which is known to alter gait compared to over-ground walking. However, the treadmill allowed for continuous walking data over three minutes without external distractions, changes to the walking surface, or a need for turns, which was necessary to assess gait variability. Another limitation is that while the present study collected falls history from our population, we did not record the cause of each individual's falls. The cause of each fall could have been beneficial in interpreting balance-related or trip-related fall risk.

This study showed that many measures of dynamic balance were different in PwMS with a history of falls compared to non-fallers with MS and healthy controls. These findings highlight distinct biomechanical differences that may explain why some PwMS experience falls and others do not. It seems in PwMS who fall, the CoM is poorly controlled through base of support placement, likely leading to an increased chance of the CoM leaving the base of support. Additionally, FA have low MTC which likely increases their risk of tripping. These findings suggest that future studies investigating gait in PwMS must consider falls history in addition to disease status. Due to the progressive and unpredictable disease course of MS, it is important to track balance dysfunction as the disease progresses in order to predict and prevent instability prior to a fall resulting in injury. These findings may lead to improved methods of quantifying and reducing fall risk in persons with multiple sclerosis.



## **Chapter 4: Dynamic balance is related to physiological impairments in persons with multiple sclerosis**

### **4.1 Abstract**

**Objectives:** To compare physiological impairments between persons with multiple sclerosis (MS) with a history of falls and persons with MS without a history of falls and to investigate the association between physiological impairments and dynamic balance.

**Design:** Cross-sectional study.

**Setting:** University motion analysis laboratory.

**Participants:** Fifty-five persons with MS (27 recurrent fallers and 28 non-fallers).

**Interventions:** None.

**Main Outcome Measures:** Physiological impairment was assessed with sensorimotor delays, spasticity, plantar cutaneous sensation, and the sensory, cerebellar, and pyramidal Expanded Disability Status Scale (EDSS) subscales. Dynamic balance was assessed using the average and variability of margin of stability and variability of trunk accelerations.

**Results:** Compared to non-fallers, fallers had lower plantar sensation, longer sensorimotor delays, more spasticity, and more impairment in the pyramidal and cerebellar EDSS subscales. Additionally, these impairments were all moderately to strongly correlated with worse dynamic balance.

**Conclusions:** The present study highlights the multifactorial nature of instability in persons with MS. A better understanding of the physiological mechanisms of dynamic instability in persons

with MS can be used to improve methods of monitoring disease progression, identifying which impairments to target through interventions, and appropriately evaluating intervention efficacy.

## **4.2 Introduction**

Approximately 500,000 people in the United States and 2.1 million worldwide have multiple sclerosis (MS) [1]. MS results in a wide variety of physiological impairments, such as slowed neural conduction speed, sensory loss, muscle weakness, and spasticity [25]. Gait and balance impairment is a major issue of persons with MS (PwMS) since over half of PwMS fall in a six month period [6] which can result in injury [6], high health care costs [1], fear of falling [3], and activity curtailment [3]. Extensive research has examined the contributions of physiological impairments to static balance [26-29], but falls most frequently occur during dynamic activities, such as walking [7]. Static and dynamic balance are controlled through different mechanisms and are often unrelated [30, 31]. Understanding the mechanisms of balance dysfunction during walking in PwMS could help design specific intervention programs to reduce fall risk, allow for a better understanding of how to evaluate intervention efficacy, and further our understanding of which physiological impairments are important to monitor through disease progression.

Gait is a complex whole-body task which requires the integration of sensory information to regulate and control many muscle groups in order to maintain forward progression and upright posture [110]. Maintaining stable gait requires active control of balance, where sensory feedback is integrated to sense the position and velocity of the center of mass (CoM) and an appropriate step placement is chosen to stabilize and redirect the CoM [55, 56]. The distance between the extrapolated (velocity-adjusted) CoM and the base of support (step placement) is

the margin of stability (MoS) [22]. PwMS walk with slower, shorter, and wider steps than healthy controls [17]. tending to increase their MoS at heel strike [9]. These gait adaptations have been speculated to be a cautious gait strategy to allow for more response time to external perturbations [9], to account for excessive and irregular trunk motions [9, 20], or to compensate for less precise control of step placement [52]. While these adaptations may represent a cautious gait, fallers with MS walk with slower [11] and wider [10] steps than non-fallers and MoS is positively correlated with number of falls [9], showing that this cautious gait strategy may actually cause instability. It has been hypothesized that maintaining a constant MoS during gait is advantageous [53] and that stride-to-stride variability of MoS reflects dynamic balance better than average MoS [45]. In PwMS, variability of both anterior-posterior (AP) and mediolateral (ML) MoS is higher in recurrent fallers compared to non-fallers and healthy controls, but similar between non-fallers and to healthy controls [111]. While MoS evaluates the interaction between the CoM and base of support, investigating the kinematic irregularities of the trunk alone is also a valid way to investigate dynamic balance [20, 60]. Nonlinear variability of trunk motion during gait, which evaluates the predictability of cyclical motion, is higher in PwMS compared to controls [20, 111] and in elderly fallers compared to elderly non-fallers [60].

Specific physiological impairments which may contribute to these dynamic balance impairments in PwMS include slowed neural conduction speed, sensory loss, muscle weakness, and spasticity [20, 27]. Sensory loss, muscle weakness, and simple reaction time tests are all related to spatiotemporal (i.e. step length, width, and time) variability in elderly individuals [112]. However, the specific relationship between these impairments and irregularities of trunk

motion during gait has not been evaluated in PwMS. Therefore, the purpose of this study is to determine if physiological impairments are different between PwMS with a history of falls and PwMS with no fall history, and examine the relationship between physiological impairments and dynamic balance in PwMS. Specific physiological impairments investigated are sensorimotor delays [27], foot vibration thresholds [28], lower extremity spasticity [29], and the pyramidal, cerebellar, and sensory EDSS subscales [11]. As PwMS with falls history have shown more impairment on sensory, pyramidal, and cerebellar EDSS subscales than non-fallers [11], and that worse physiological impairments are related to poor static balance in PwMS [27-29], we hypothesize that physiological impairments will be higher in fallers compared to non-fallers and will correlate with poor dynamic balance.

### **4.3 Methods**

#### **4.3.1 Participants**

Fifty-five PwMS were included in the present study (Table 1). The University of Kansas Medical Center Human Research Committee approved this study and all participants gave informed written consent. All subjects were between the ages of 21-60, had relapsing remitting MS, and had an EDSS score less than 5.5. The self-reported number of falls in the six months prior to data collection was recorded. PwMS were classified as non-fallers if they did not experience a fall in the previous 6 months (n=28) and as fallers if they experienced 2 or more falls in the previous 6 months (n=27), as PwMS who fall more than once are more likely to have fallen due to intrinsic disease specific factors [10], Demographics were compared between groups using paired t-tests (Table 5).

**Table 5:** Sample demographics for the entire population (n = 55), non-fallers (n=27), and faller (n=28) groups, and t-tests comparing non-fallers and fallers. Abbreviations: BMI – Body mass index; 25FTW – timed 25 foot walk; EDSS – Kurtzke’s expanded disability status scale.

	<b>All (n=55)</b>	<b>PwMS</b>	<b>Non-fallers (n=28)</b>	<b>Fallers (n=27)</b>	<b>Independent t-tests</b>
Age	46.2 (9.7)		45.9 (9.5)	46.6 (10.1)	1.000
Gender (F/M)	39/16		20/8	19/8	-
BMI	28.3 (7.4)		28.0 (6.5)	28.6 (8.4)	1.000
T25FW (sec)	5.5 (1.6)		4.7 (0.9)	6.3 (1.8)	<b>&lt;0.001</b>
EDSS	2.3 (1.2)		1.8 (0.9)	2.8 (1.2)	<b>0.001</b>
Berg Balance Scale	51.9 (6.3)		54.11 (3.07)	49.63 (7.81)	<b>0.007</b>
Years since diagnosis	11.1 (8.5)		10.5 (8.5)	11.7 (8.5)	0.625
Falls in previous 6 months	3.8 (9.5)		0.0 (0.0)	7.8 (12.5)	<b>0.002</b>
Preferred Walking Speed (m/s)	1.62 (0.29)		0.73 (0.23)	0.51 (0.30)	<b>0.012</b>

#### 4.3.2 Gait protocol and analysis

All subjects walked on a treadmill at their self-selected preferred pace for 3 minutes. Kinematic data<sup>a</sup> was collected at 60 Hz using retroreflective markers placed bilaterally on the anterior and posterior superior iliac spine, heel, lateral malleolus, top of the second metatarsal phalangeal joint, and at the lateral metatarsal phalangeal. Wireless inertial sensors<sup>b</sup> measured trunk accelerations at 128 Hz, placed over the midline of the sternum, inferior to the manubrium and superior to the xiphoid process.

Heel strikes were defined as the AP local maxima from the heel marker’s trajectory. MoS was calculated as the distance between the extrapolated CoM and base of support [22], which has been described in detail elsewhere [9, 45]. The position of the CoM was estimated using the geometric center of the pelvic markers, and the edge of the base of support in the AP and ML

direction was estimated using the toe and lateral MTP markers respectively [9, 45]. MoS was calculated in the AP and ML direction at each heel strike and averaged over the whole trial. The number of steps per trial ranged from 79 to 175, with non-fallers walking significantly faster than fallers ( $p=0.012$ ) (Table 1). MoS variability was assessed using coefficient of variation, which represents the standard deviation normalized by the average [12]. Average MoS and MoS variability were calculated independently for the left and right leg and averaged for each subject.

Linear trunk accelerations were measured in the AP, ML, and vertical (VT) axis, and analyzed independently. Root mean square transforms (RMS) were used to describe the dispersion of each signal [20, 78]. Temporal structure of trunk accelerations was assessed with Lyapunov Exponents (LyE) and Sample Entropy (SaEn). Raw acceleration time series were down-sampled to 60 Hz and truncated to the middle 60 strides [97]. Delay-embedded state spaces were reconstructed independently in each axis. Embedding dimensions were found using the global false nearest neighbor algorithm, and time delays were found using the average mutual information algorithm [97]. Both algorithms were used on each independent time series, and the median of every subject resulted in an embedding dimension of 7 for each axis, and time delays of 6, 8, and 9 for the AP, ML, and VT axis, respectively [97]. LyE were calculated using Wolf's algorithm. SaEn [98] was calculated with the medium time delays from the average mutual information analysis [78]. Values of  $m=3$  and  $r=0.2$  were used, as these have been found to be robust for SaEn calculations of trunk accelerations [78].

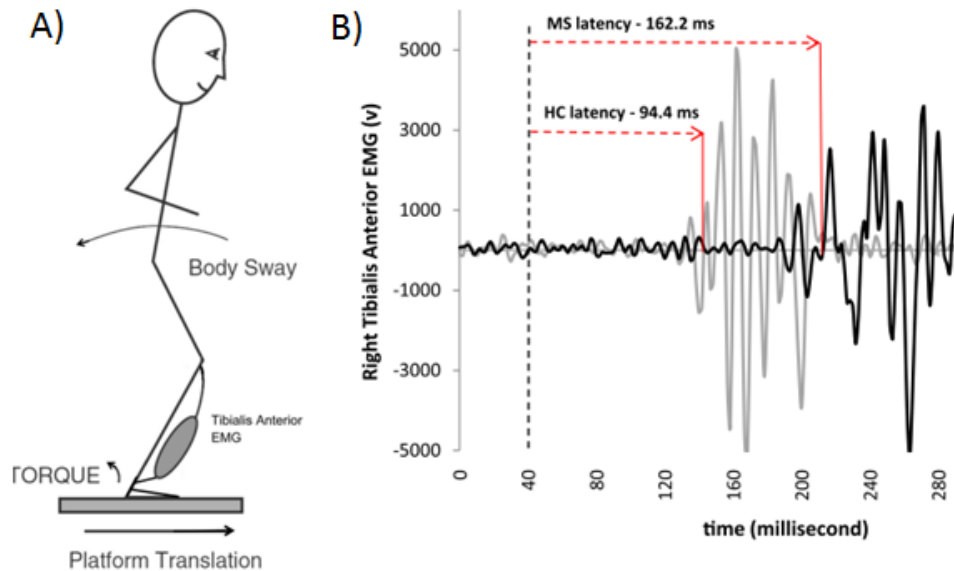
#### **4.3.3 Physiological deficits protocol and analysis**

##### *Foot vibration threshold*

Vibration threshold the big toe was assessed using the Vibratron II<sup>c</sup> device [88], where the lowest amplitude of vibration detectable was recorded for the left and right foot and averaged for each subject.

#### *Sensorimotor delays*

Each subject stood on a servo-controlled motorized treadmill<sup>d</sup>, which translated forward causing a backwards body sway [84]. The treadmill translated approximately 4-6 cm at approximately 4 cm/s. Wireless surface electromyography sensors<sup>e</sup> were placed bilaterally over the tibialis anterior. Electromyography signals were sampled at 1800 Hz amplified, band-pass filtered (70-2000 Hz), and stored for off-line analysis. Sensorimotor delays were defined as the time between treadmill onset and the first measurable increase in electromyography activity greater than 2 SD from baseline that was sustained for at least 50 milliseconds [27, 84]. Latencies for 3 separate trials including both legs were averaged for each subject.



**Figure 6:** A) Illustration of the experimental setup for postural perturbations using the translating force platform. B) Graphical representation of the calculation of sensorimotor delays. Abbreviations: EMG – electromyography; MS – multiple sclerosis; HC – healthy controls [27].

### *Spasticity*

Lower limb spasticity was assessed bilaterally in the hamstring, quadriceps, and plantarflexors using the modified Ashworth scale [29], which was scored between 0 (no increase in muscle tone) and 4 (the affected part is rigid). Spasticity was documented as the average score across all three muscle groups bilaterally for each subject.

### *EDSS subscales*

Disease severity was assessed with the Kurtzke's expanded disability status scale (EDSS), administered by a neurologist (author SL) [113]. The pyramidal, cerebellar, and sensory subscale scores were recorded.

### **4.3.4 Statistical analysis**

As many outcome measures chosen were found to be non-normally distributed, non-



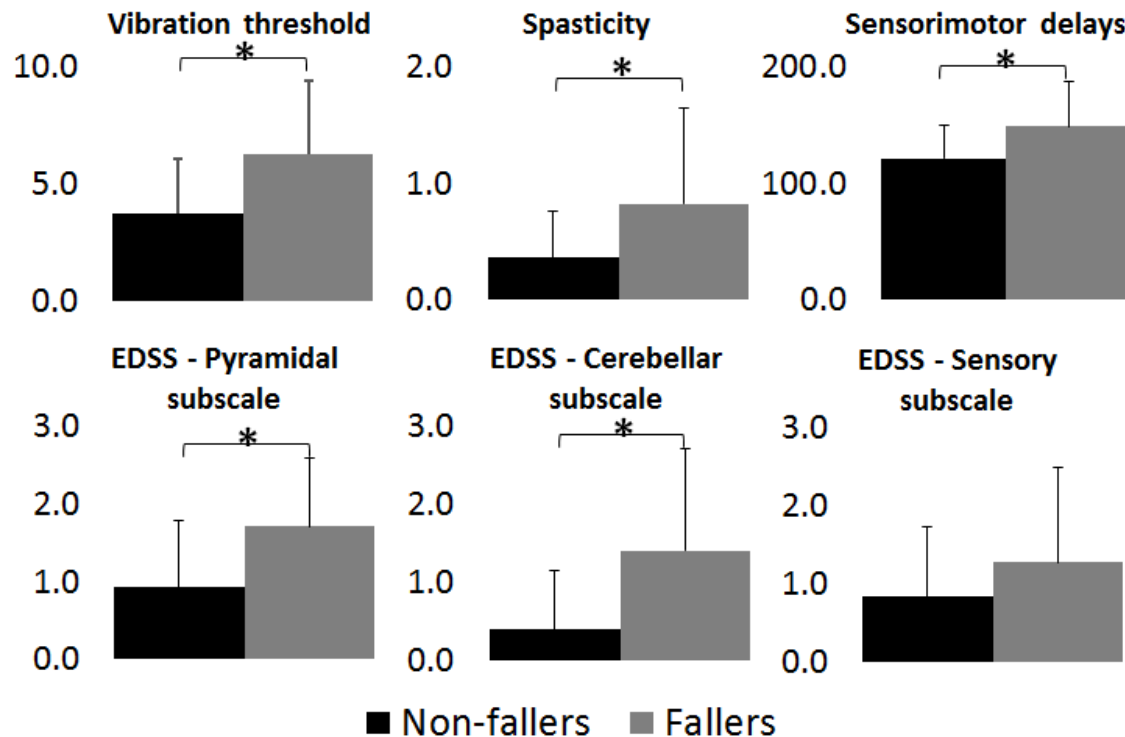
parametric statistical tests were used. Physiological impairments were compared between fallers and non-fallers with MS using Mann-Whitney U-Tests. The relationship between physiological impairment measures and dynamic balance measures were assessed across all subjects with MS using spearman's rank correlation coefficients. All statistics were performed with SPSS software.<sup>f</sup> Significance was set at 0.05.

#### 4.4 Results

Compared to non-fallers, fallers had a higher vibration threshold ( $p=0.003$ ), longer sensorimotor delays ( $p=0.002$ ), more spasticity ( $p=0.017$ ), and more impairment in the pyramidal ( $p=0.002$ ) and cerebellar EDSS subscales ( $p=0.003$ ) (Table 6; Figure 7).

**Table 6:** Physiological impairment differences between fallers and non-fallers; values are presented as Median (IQR), with z- and p-values based on Mann-Whitney U Test.

	Non-Fallers (n=28)	Fallers (n=26)	Z	p
<b>Vibration Threshold</b>	3.0 (2.0)	5.5 (5.2)	<b>-2.972</b>	<b>0.003</b>
<b>Sensorimotor Delays</b>	118.57 (25.65)	143.20 (41.43)	<b>-3.131</b>	<b>0.002</b>
<b>Spasticity</b>	0.33 (0.66)	0.66 (0.66)	<b>-2.397</b>	<b>0.017</b>
<b>Pyramidal</b>	1 (1)	2 (1)	<b>-3.054</b>	<b>0.002</b>
<b>Cerebellar</b>	0 (1)	1 (2.5)	<b>-2.958</b>	<b>0.003</b>
<b>Sensory</b>	1 (1)	1 (2)	-1.223	0.221



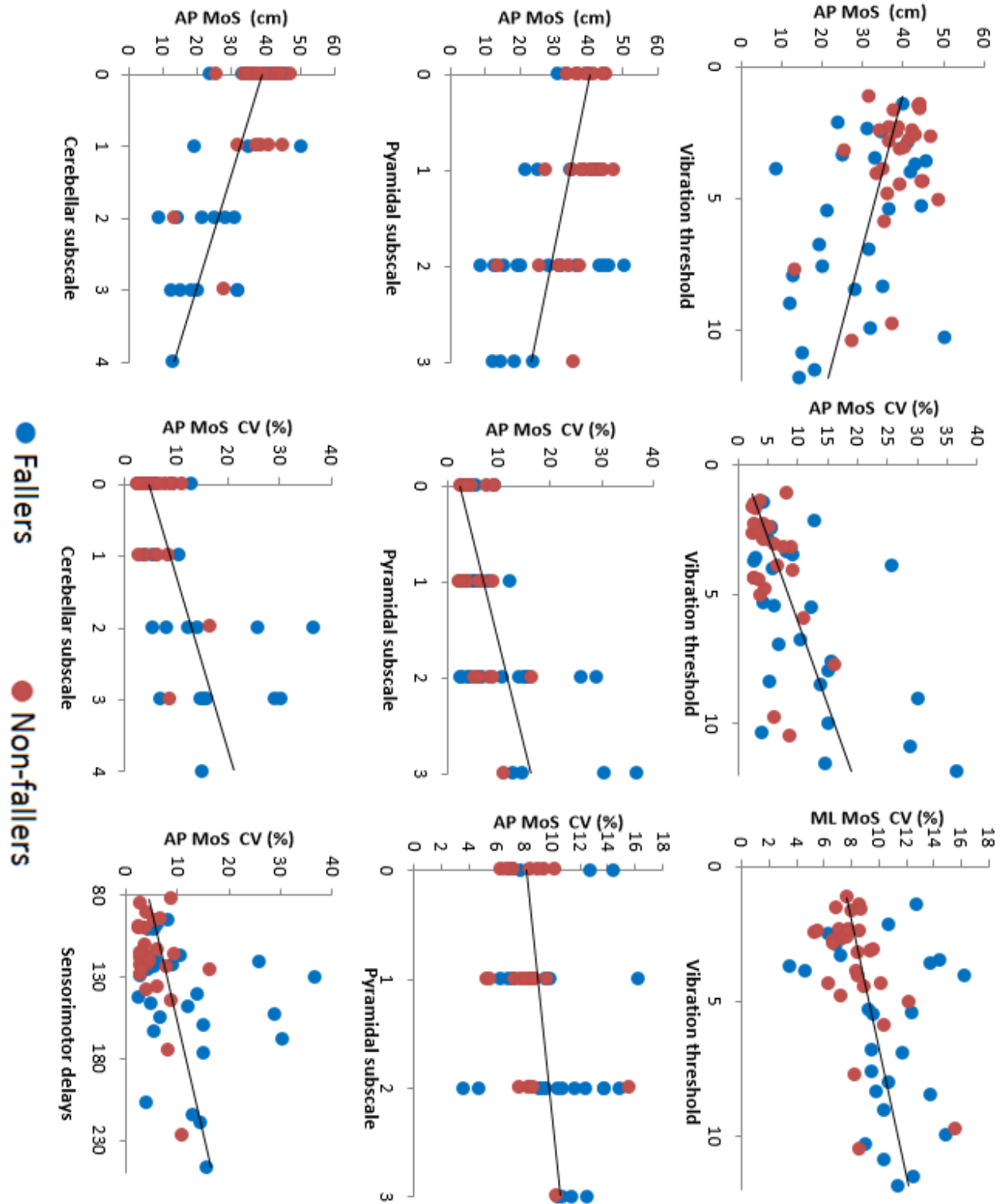
**Figure 7:** Comparison of physiological impairment between persons with MS who are non-fallers (NF) and persons with MS who are fallers (FA). \* represents significant difference between groups ( $p < 0.05$ ).

Correlations between physiological impairments and dynamic balance measures can be found in Table 7 and Table 8 (Figure 8; Figure 9). Vibration thresholds were significantly correlated with average AP MoS ( $r = -0.393$ ), AP ( $r = 0.568$ ) and ML ( $r = 0.507$ ) MoS coefficient of variation, LyE of ML trunk accelerations ( $r = 0.408$ ), and RMS ( $r = -0.355$ ), LyE ( $r = 0.284$ ), and SaEn ( $r = 0.273$ ) of VT trunk accelerations. Sensorimotor delays were significantly correlated with average AP MoS ( $r = -0.292$ ), AP ( $r = 0.440$ ) and ML ( $r = 0.314$ ) MoS coefficient of variation, LyE of ML trunk accelerations ( $r = 0.277$ ), and RMS ( $r = -0.355$ ), LyE ( $r = 0.378$ ), and SaEn ( $r = 0.299$ ) of VT trunk accelerations. Spasticity scores were significantly correlated with average AP MoS ( $r = -0.346$ ), AP MoS coefficient of variation ( $r = 0.339$ ), and RMS ( $r = -0.334$ ) and SaEn ( $r = 0.309$ ) of VT trunk accelerations. Pyramidal EDSS subscale scores were significantly correlated with average

AP MoS ( $r=-0.456$ ), AP ( $r=0.556$ ) and ML ( $r=0.384$ ) MoS coefficient of variation, and RMS ( $r=-0.485$ ), LyE ( $r=0.334$ ), and SaEn ( $r=0.477$ ) of VT trunk accelerations. Cerebellar EDSS subscale scores were significantly correlated with average AP MoS ( $r=-0.662$ ), AP MoS coefficient of variation ( $r=0.639$ ), RMS ( $r=-0.316$ ) and LyE ( $r=0.344$ ) of ML trunk accelerations, and RMS ( $r=-0.451$ ), LyE ( $r=0.412$ ), and SaEn ( $r=0.472$ ) of VT trunk accelerations. Sensory EDSS subscale scores were significantly correlated with AP MoS coefficient of variation ( $r=0.315$ ) and average ML MoS ( $r=0.283$ ).

**Table 7:** Correlations between sensorimotor impairment measures and MoS dynamic balance measures. Abbreviations: AP – Anterior-posterior; ML – Mediolateral; MoS – Margin of stability; CV – coefficient of variation. Values are presented as correlation coefficient (P). Significant difference indication: \*  $p < .001$ ; \*\*  $p < .01$ ; \*\*\*  $p < .05$ .

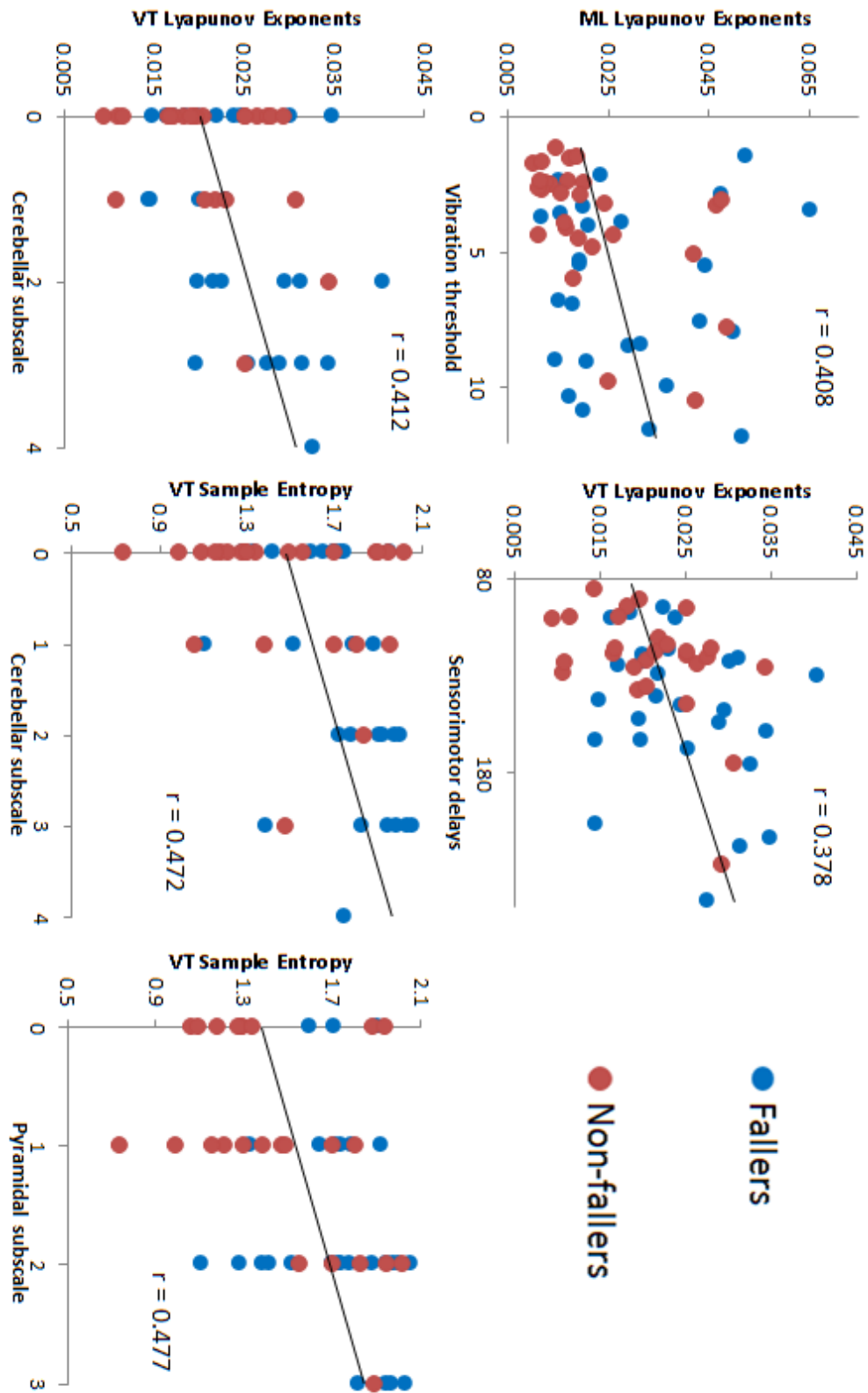
	AP MoS (cm)	AP MoS CV (%)	ML MoS (cm)	ML MoS CV (%)
<b>Vibration Threshold</b>	<b>-0.393</b> <b>(0.003)***</b>	<b>0.568</b> <b>(&lt;0.001)***</b>	-0.039 (0.782)	<b>0.507</b> <b>(&lt;0.001)***</b>
<b>Sensorimotor Delays</b>	<b>-0.292</b> <b>(0.032)*</b>	<b>0.440</b> <b>(0.001)***</b>	0.134 (0.336)	<b>0.314</b> <b>(0.021)*</b>
<b>Spasticity</b>	<b>-0.346</b> <b>(0.011)*</b>	<b>0.339</b> <b>(0.013)*</b>	-0.130 (0.353)	0.100 (0.477)
<b>Pyramidal</b>	<b>-0.456</b> <b>(0.001)***</b>	<b>0.556</b> <b>(&lt;0.001)***</b>	0.045 (0.755)	<b>0.384</b> <b>(0.005)***</b>
<b>Cerebellar</b>	<b>-0.662</b> <b>(&lt;0.001)***</b>	<b>0.639</b> <b>(&lt;0.001)***</b>	-0.025 (0.859)	0.259 (0.067)
<b>Sensory</b>	-0.260 (0.072)	<b>0.315</b> <b>(0.027)*</b>	<b>0.283</b> <b>(0.049)*</b>	0.248 (0.086)



**Figure 8:** Correlation between physiological impairment measures and margin of stability (MoS) measures. Abbreviation: CV – coefficient of variation.

**Table 8:** Correlations between sensorimotor impairment measures and nonlinear trunk variability measures. Abbreviations: AP – Anterior-posterior; ML – Medial-lateral; VT – Vertical; RMS – root mean square; LyE – Lyapunov exponents; SaEn – Sample entropy. Values are presented as correlation coefficient (P). Significant difference indication: \* p < .001; \*\* p < .01; \*\*\* p < .05.

	AP LyE	ML LyE	VT LyE	AP SaEn	ML SaEn	VT SaEn	AP RMS	ML RMS	VT RMS
<b>Vibration Threshold</b>	-0.013 (0.929)	<b>0.408</b> (0.002)***	<b>0.284</b> (0.038)*	0.045 (0.747)	0.217 (0.111)	<b>0.273</b> (0.043)*	0.089 (0.520)	-0.178 (0.192)	<b>-0.335</b> (0.013)*
<b>Sensorimotor Delays</b>	0.199 (0.158)	<b>0.277</b> (0.041)*	<b>0.378</b> (0.005)***	0.016 (0.908)	0.098 (0.479)	<b>0.299</b> (0.027)*	0.018 (0.897)	0.152 (0.268)	<b>-0.355</b> (0.008)*
<b>Spasticity</b>	0.119 (0.401)	0.150 (0.279)	0.214 (0.124)	0.019 (0.892)	0.189 (0.171)	<b>0.309</b> (0.023)*	-0.067 (0.629)	-0.214 (0.120)	<b>-0.334</b> (0.015)*
<b>Pyramidal</b>	0.202 (0.160)	0.125 (0.367)	<b>0.334</b> (0.017)*	0.189 (0.179)	-0.143 (0.312)	<b>0.477</b> (<0.001)***	-0.093 (0.510)	-0.105 (0.459)	<b>-0.485</b> (<0.001)** *
<b>Cerebellar</b>	0.180 (0.212)	<b>0.344</b> (0.013)*	<b>0.412</b> (0.003)***	-0.026 (0.857)	0.218 (0.120)	<b>0.472</b> (<0.001)***	0.064 (0.651)	<b>-0.316</b> (0.023)*	<b>-0.451</b> (0.001)***
<b>Sensory</b>	0.195 (0.180)	-0.002 (0.988)	0.196 (0.177)	-0.051 (0.726)	-0.099 (0.493)	0.214 (0.136)	0.170 (0.239)	-0.113 (0.433)	-0.265 (0.066)



**Figure 9:** Correlation between physiological impairment measures and trunk acceleration variability. ML – mediolateral; VT – vertical.

## 4.5 Discussion

The purpose of the present study was to determine if physiological impairments are different between PwMS with a history of falls and PwMS with no fall history, and to examine the relationship between physiological impairments and dynamic balance in PwMS. We hypothesized that fallers would be more physiologically impaired than non-fallers and that greater physiological impairment would correlate with worse dynamic balance. The results of the present study support these hypotheses. As many distinct physiological impairments were found to differentiate fallers from non-fallers with MS and to correlate with dynamic balance, the results of the present study highlight the multifactorial nature of instability in this population and suggest that a combination of impairments is likely a major contributor to dynamic instability and falls. These findings provide novel information relating distinct physiological impairments to dynamic instability in PwMS.

Sensorimotor delays were longer in fallers than non-fallers and were moderately correlated with dynamic balance. Sensorimotor delays evaluate the combined somatosensory and motor response times after a translational postural perturbation so any delay in sensorimotor response time represents both sensory and motor tract conduction impairments [84, 114]. This is true in the present study since post-hoc spearman's rank correlations show that sensorimotor delays are correlated with both the sensory ( $\rho=0.555$ ,  $p<0.001$ ) and pyramidal ( $\rho=0.484$ ,  $p<0.001$ ) EDSS subscales. Lyapunov exponents quantify a systems sensitivity to small local perturbations during gait [115]. Deviations in center of mass kinematics (also considered perturbations) during gait are corrected through appropriate step placement [55]. Sensorimotor delays correlated with both Lyapunov exponents of trunk accelerations and

MoS variability, showing that individuals with longer sensorimotor delays to postural perturbations during stance also have a decreased ability to correct center of mass deviations during gait and thus have poor dynamic balance and a likely increased risk for falling. Slower walking speeds with lower magnitudes of trunk accelerations, demonstrated by lower trunk acceleration RMS in individuals with longer sensorimotor delays, are likely a compensatory strategy to preserve stability in PwMS. These results highlight the importance of quick neural conduction for maintaining balance, and show that slowed neural conduction speed in PwMS compromises dynamic balance.

Foot vibration thresholds were found to be worse in fallers compared to non-fallers and were moderately correlated with dynamic balance measures, indicating that fallers have worse plantar sensation than non-fallers and that less sensation is associated with poor dynamic balance. Healthy individuals with experimentally numbed feet and persons with diabetic peripheral neuropathy also have decreased cutaneous sensitivity and increased gait variability which demonstrates the independent contribution of plantar sensation to dynamic balance [87, 116]. Less somatosensory feedback in PwMS likely leads to a poor perception of their center of mass kinematics, which is shown here to relate to dynamic instability and falls. However, the sensory EDSS subscale did not differ between fallers and non-fallers and only weakly correlated with AP MoS coefficient of variation and average ML MoS in the present study, which may indicate limited sensitivity of the sensory EDSS subscale to plantar sensation. Previous work found that 30% of PwMS who had normal sensory EDSS subscale scores had cutaneous vibration thresholds outside of 2.5 SD of age matched controls [88], which may be due to subjective and variable measures of vibration sensitivity used on the EDSS [117]. Additionally,



previous work found no relationship between proprioception acuity and gait variability [12] or fall risk [118] in PwMS using a lower limb matching task. It is unclear if discrepancies found relating somatosensory acuity to dynamic instability and falls in PwMS is due to differences in instrumentation sensitivity or the specific sensory receptors examined. Future work should aim to document specific impairments found in different sensory systems in PwMS and evaluate their individual contributions to instability.

In the present study, the pyramidal EDSS subscale scores were higher in fallers compared to non-fallers and correlated moderately with dynamic balance measures. Motor impairment is very common in PwMS and is characterized by slowed force production rates, weaker maximal force production, less control of force production, spasticity, and fatigue [10, 25, 92]. Lower limb spasticity was greater in fallers compared to non-fallers and was moderately correlated with dynamic balance measures, particularly in the AP direction. While the present study tested spasticity in muscles primarily used for sagittal plane propulsion, spasticity in other muscle groups, such as hip abductors, may have associated with frontal plane dynamic balance. In general, the correlations between dynamic balance and the pyramidal EDSS subscale were stronger than between dynamic balance and spasticity alone, which means that other motor impairments such as muscle weakness and fatigue likely contributed to dynamic instability during gait. The present study highlights a need for a better understanding of how motor impairments affect dynamic balance and falls in PwMS.

Cerebellar involvement was greater in fallers than non-fallers, and was found to strongly correlate with dynamic balance measures. The cerebellar EDSS subscale is examined through tests of fine motor control and balance, such as alternating finger to nose movements and

tandem standing and walking. Previous reports have shown that similar tests of fine motor control significantly contributed to differentiating frequent fallers from infrequent fallers with MS [118]. PwMS can develop cerebellar lesions. An MRI study by Prosperini et al found a larger lesion load in the cerebellum in fallers compared to non-fallers, which correlated with poor static balance [26]. Cerebellar damage is known to result in slower walking with a wider base of support, variable foot placement, and abnormal joint coordination, which may be caused by a decreased ability to modulate the timing and amplitude of rhythmic muscular activity [119]. Persons with focal cerebellar lesions are known to have an increased amount of lateral instability [120]; however in the present study cerebellar involvement only weakly correlated with LyE in the ML direction. Because the cerebellar EDSS subscale did not correlate with ML MoS variability, these two measures may be providing different information about the physiological control of dynamic balance. The present results indicate that cerebellar damage likely influences dynamic instability; however our present study design is insufficient to determine whether the cerebellar EDSS subscale scores were influenced by other physiological impairments.

### *Study limitations*

A limitation of our experimental procedure was the use of a treadmill for data collection, which is known to alter gait compared to over-ground walking. Some PwMS likely had little experience walking on a treadmill, resulting in a potentially novel task that may not have accurately described their natural over-ground gait. However, the treadmill allowed for continuous walking data over three minutes without external distractions, changes to the walking surface, or a need for turns. Additionally, while significant relationships between

physiological impairment and instability were observed in the present study, correlations were weak to moderate ( $p=.283-.639$ ), indicating that other impairments may contribute to the problem of instability.

## **Conclusion**

Distinct physiological impairments found in PwMS are related to dynamic balance. Also, physiological impairments are more severe in PwMS who fall compared to PwMS who have a falls history. These results highlight the multifactorial nature of dynamic instability in PwMS and suggest that instability likely arises from deficits in the ability to quickly and accurately sense local inter-stride deviations in center of mass positioning and motion and from motor or cerebellar impairments which may increase the frequency and magnitude of center of mass deviations. Evaluating dynamic balance and distinct physiological impairments may provide useful indicators of disease progression, aid in individualizing therapies for intervention, and improve measurement of responsiveness to intervention. Targeting specific physiological impairments through intervention programs may improve dynamic balance and reduce fall risk in PwMS.

## **Suppliers**

- a. Motion Analysis, 3617 Westwind Blvd, Santa Rosa, CA 95403
- b. Opal, APDM, 2828 SW Corbett Avenue, Portland, OR 97201
- c. Vibratron II, Physitemp, 154 Huron Avenue, Clifton, New Jersey 07013
- d. Bari-Mill, Woodway, W229 N591 Foster Ct., Waukesha, WI 53186
- e. Delsys, 23 Strathmore Road, Natick, Massachusetts 01760
- f. IBM SPSS Statistics, 1 New Orchard Rd, Armonk, NY 10504.

## Chapter 5: Conclusion and Future Work

The first purpose of this study was to identify distinct features of dynamic balance during gait which were different between PwMS who have a history of falls, PwMS with no history of falls, and healthy controls. While previous work has compared either foot motion [17] or trunk motion [20] between PwMS and HC, or foot motion between fallers and non-fallers with MS [13], no previous study has compared dynamic balance between fallers and non-fallers with MS. The present study found that fallers with MS have worse dynamic balance than both non-fallers and healthy controls, which may help explain why these individuals experience falls. Specifically, fallers with MS have a reduced ability to control the center of mass through base of support placement and have lower foot clearances during swing. Through evaluating gait during routine clinical visits in PwMS, these dynamic balance measures may be able to not only quantify an individual's risk for falling during gait, but describe the risk (i.e. poor later balance or low toe clearance). Body worn wireless sensors such as inertial measurement units are inexpensive, noninvasive, and portable, making them advantageous for objectively quantifying mobility and balance in clinical environments. Future work should therefore develop measures aimed at quantifying the identified altered movement patterns observed in fallers with MS in the present study using wireless sensors. While calculating MoS requires motion capture technology, which is not clinically feasible, a possible alternative method of examining the accuracy of step placements could be examining the stride-to-stride relationship between center of mass motion and foot motion during swing phase using wireless sensors [51]. The results of the present study suggest that focusing on restoring healthy step placements to control the center of mass and increasing foot clearance during swing phase

could be the most effective ways to prevent falls in PwMS. Strategies that focus on guiding appropriate step placements [104, 105] or controlling the center of mass during various static and dynamic task with varying sensory feedback manipulations [106, 107] may improve dynamic balance and reduce the risk of falls. Additionally, a dynamic balance biofeedback rehabilitation program may be able to target and improve specific features of fall risk (i.e. poor lateral balance or low toe clearance). Biofeedback rehabilitation approaches typically measure some aspect of human movement, such as postural sway or electromyography, and presents the measurement to the individual through a visual display. This approach allows patients to visualize specific movement features which they may not be aware of, like how much they are swaying during quiet stance, and often provides individuals with a task-specific goal such as reducing sway. While use of biofeedback in PwMS has been limited, biofeedback has increased ankle propulsion in elderly individuals [121] and hemiplegic individuals [122], reduced postural sway in persons with vestibular loss [123], and increase toe clearance in elderly individuals [124]. If margin of stability or toe clearance was measured and presented to PwMS in real-time, they may become more aware of their fall risk and could be trained to walk safer.

The second purpose of this study was to determine if physiological impairments are different between PwMS with a history of falls and PwMS with no fall history, and examine the relationship between physiological impairments and dynamic balance in PwMS. Results show that more severe physiological impairments are associated with worse dynamic balance in PwMS and that fallers with MS have more severe impairments than non-fallers. These results highlight the multifactorial nature of dynamic instability in PwMS, suggesting that instability likely arises from the inability to quickly and accurately sense local inter-stride deviations in

center of mass motion, as well as from motor or cerebellar impairments which may increase the frequency and magnitude of center of mass deviations. A future study designed to evaluate the independent contribution of distinct physiological impairments to dynamic instability using a more comprehensive set of objective sensory and motor impairment metrics, sensorimotor delays, and central nervous system imaging techniques in a regression analysis would be beneficial. Specific sensory impairments to investigate include lower limb joint position sense (such as hip abductors), cutaneous sensitivity, and visual acuity. Motor impairments to investigate include maximum force production, maximum rate of force production, control of muscular force development, spasticity, and fatigue. Imaging techniques are able to identify localized damage in distinct structures of the central nervous system, such as the cerebellum [26] and spinal cord pathways [125], and could help in identifying the mechanisms of physiological impairment and their contribution to dynamic instability. Current FDA approved medications target specific physiological impairments, such as spasticity or nerve conduction speed [126]. Future work should investigate how different medications effect dynamic balance in PwMS. As these physiological impairments often develop and worsen with disease progression, experimental studies alone make it difficult to tease the individual contribution of specific impairments to instability. Computational models of feedback controlled dynamic walkers are able to resemble both healthy and pathological human gait. By systematically altering individual model parameters we may be able to gain further insight into the independent contribution of distinct physiological impairments to gait instability [127]. Lastly, rehabilitation research should use specific instrumented measures of dynamic balance and physiological impairment to further our understanding of symptom management.

## References

- [1] Campbell JD, Ghushchyan V, Brett McQueen R, Cahoon-Metzger S, Livingston T, Vollmer T, et al. Burden of multiple sclerosis on direct, indirect costs and quality of life: National US estimates. *Multiple sclerosis and related disorders*. 2014;3:227-36.
- [2] Finlayson ML, Peterson EW, Cho CC. Risk factors for falling among people aged 45 to 90 years with multiple sclerosis. *Archives of physical medicine and rehabilitation*. 2006;87:1274-9; quiz 87.
- [3] Peterson EW, Cho CC, Finlayson ML. Fear of falling and associated activity curtailment among middle aged and older adults with multiple sclerosis. *Multiple Sclerosis*. 2007;13.
- [4] Nilsagard Y, Lundholm C, Denison E, Gunnarsson L. Predicting accidental falls in people with multiple sclerosis -- a longitudinal study. *Clinical rehabilitation*. 2009;23.
- [5] Peterson EW, Cho CC, von Koch L, Finlayson ML. Injurious falls among middle aged and older adults with multiple sclerosis. *Archives of physical medicine and rehabilitation*. 2008;89:1031-7.
- [6] Matsuda PN, Shumway-Cook A, Bamer AM, Johnson SL, Amtmann D, Kraft GH. Falls in multiple sclerosis. *PM & R : the journal of injury, function, and rehabilitation*. 2011;3:624-32; quiz 32.
- [7] Peterson EW, Ben Ari E, Asano M, Finlayson ML. Fall attributions among middle-aged and older adults with multiple sclerosis. *Archives of physical medicine and rehabilitation*. 2013;94:890-5.
- [8] Gunn H, Creanor S, Haas B, Marsden J, Freeman J. Frequency, characteristics, and consequences of falls in multiple sclerosis: findings from a cohort study. *Archives of physical medicine and rehabilitation*. 2014;95:538-45.
- [9] Peebles AT, Reinholdt A, Bruetsch AP, Lynch SG, Huisinga JM. Dynamic margin of stability during gait is altered in persons with multiple sclerosis. *Journal of biomechanics*. 2016;49:3949-55.
- [10] Kasser SL, Jacobs JV, Foley JT, Cardinal BJ, Maddalozzo GF. A prospective evaluation of balance, gait, and strength to predict falling in women with multiple sclerosis. *Archives of physical medicine and rehabilitation*. 2011;92:1840-6.
- [11] Sosnoff JJ, Michael J. Socie, Morgan K. Boes, Brian M. Sandroff, John H. Pula, Yoojin Suh, et al. Mobility, Balance and Falls in Persons with Multiple Sclerosis. *PloS one*. 2011;6.
- [12] Moon Y, Wajda DA, Motl RW, Sosnoff JJ. Stride-Time Variability and Fall Risk in Persons with Multiple Sclerosis. *Mult Scler Int*. 2015;2015:964790.
- [13] Socie MJ, Sandroff BM, Pula JH, Hsiao-Weckler ET, Motl RW, Sosnoff JJ. Footfall placement variability and falls in multiple sclerosis. *Annals of biomedical engineering*. 2013;41:1740-7.
- [14] Benedetti M, Piperno R, Simoncini L, Bonato P, Tonini A, Giannini S. Gait abnormalities in minimally impaired multiple sclerosis patients. *Multiple Sclerosis*. 1999;5:363-8.
- [15] Kelleher KJ, Spence W, Solomonidis S, Apatsidis D. The characterisation of gait patterns of people with multiple sclerosis. *Disability and rehabilitation*. 2010;32:1242-50.
- [16] Martin C, Phillips B, Kilpatrick T, Butzkueven H, Tubridy N, McDonald E, et al. Gait and balance impairment in early multiple sclerosis in the absence of clinical disability. *Multiple Sclerosis*. 2006;12.
- [17] Sosnoff JJ, Sandroff BM, Motl RW. Quantifying gait abnormalities in persons with multiple sclerosis with minimal disability. *Gait & posture*. 2012;36:154-6.
- [18] Socie MJ, Motl RW, Sosnoff JJ. Examination of spatiotemporal gait parameters during the 6-min walk in individuals with multiple sclerosis. *International journal of rehabilitation research Internationale Zeitschrift fur Rehabilitationsforschung Revue internationale de recherches de readaptation*. 2014;37:311-6.
- [19] Crenshaw SJ, Royer TD, Richards JG, Hudson DJ. Gait variability in people with multiple sclerosis. *Multiple Sclerosis*. 2006.
- [20] Huisinga JM, Mancini M, St George RJ, Horak FB. Accelerometry reveals differences in gait variability between patients with multiple sclerosis and healthy controls. *Annals of biomedical engineering*. 2013;41:1670-9.

- [21] Kaipust JP, Huisinga JM, Filipi ML, Stergiou N. Gait variability measures reveal differences between multiple sclerosis patients and healthy controls. *Motor control*. 2012;16:229-44.
- [22] Hof AL, Gazendam MG, Sinke WE. The condition for dynamic stability. *Journal of biomechanics*. 2005;38:1-8.
- [23] Karmakar C, Khandoker A, Begg R, Palaniswami M. Understanding ageing effects using complexity analysis of foot-ground clearance during walking. *Computer methods in biomechanics and biomedical engineering*. 2013;16:554-64.
- [24] Byju AG, Nussbaum MA, Madigan ML. Alternative measures of toe trajectory more accurately predict the probability of tripping than minimum toe clearance. *Journal of biomechanics*. 2016;49:4016-21.
- [25] Noseworthy JH, Lucchinetti C, Rodrigues M, Weinshenker BG. Multiple Sclerosis. *New England Journal of Medicine*. 2000;938-52.
- [26] Prosperini L, Kouleridou A, Petsas N, Leonardi L, Tona F, Pantano P, et al. The relationship between infratentorial lesions, balance deficit and accidental falls in multiple sclerosis. *Journal of the neurological sciences*. 2011;304:55-60.
- [27] Huisinga JM, St George RJ, Spain R, Overs S, Horak FB. Postural response latencies are related to balance control during standing and walking in patients with multiple sclerosis. *Archives of physical medicine and rehabilitation*. 2014;95:1390-7.
- [28] Citaker S, Gunduz AG, Guclu MB, Nazliel B, Irkec C, Kaya D. Relationship between foot sensation and standing balance in patients with multiple sclerosis. *Gait & posture*. 2011;34:275-8.
- [29] Sosnoff JJ, Gappmaier E, Frame A, Motl RW. Influence of Spasticity on Mobility and Balance in Persons With Multiple Sclerosis. *Journal of Neurologic Physical Therapy*. 2011;35:129-32.
- [30] Kang HG, Dingwell JB. A direct comparison of local dynamic stability during unperturbed standing and walking. *Experimental brain research*. 2006;172:35-48.
- [31] Hausdorff J, Nelson M, Kaliton D, Layne J, Bernstein M, Nuernberger A, et al. Etiology and modification of gait instability in older adults: a randomized controlled trial of exercise. *Journal of Applied Physiology*. 2001;90:2117-29.
- [32] What is MS. <http://www.nationalmssociety.org>: National Multiple Sclerosis Society.
- [33] Smith KJ, McDonald WI. The pathophysiology of multiple sclerosis: the mechanisms underlying the production of symptoms and the natural history of the disease. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*. 1999;354:1649-73.
- [34] Vickrey B, Hays RD, Harooni R, Myers LW, Ellison GW. A Health-Related Quality of Life Measure for Multiple Sclerosis. *Quality of life research*. 1995;4:187-206.
- [35] Prosperini L, Fortuna D, Gianni C, Leonardi L, Pozzilli C. The diagnostic accuracy of static posturography in predicting accidental falls in people with multiple sclerosis. *Neurorehabilitation and neural repair*. 2013;27:45-52.
- [36] Chung LH, Remelius JG, Van Emmerik RE, Kent-Braun JA. Leg power asymmetry and postural control in women with multiple sclerosis. *Med Sci Sports Exerc*. 2008;40:1717-24.
- [37] Kalron A, Givon U. Gait characteristics according to pyramidal, sensory and cerebellar EDSS subcategories in people with multiple sclerosis. *J Neurol*. 2016;263:1796-801.
- [38] Preiningerova JL, Novotna K, Ruzs J, Sucha L, Ruzicka E, Havrdova E. Spatial and temporal characteristics of gait as outcome measures in multiple sclerosis (EDSS 0 to 6.5). *Journal of Neuroeng Rehabil*. 2015;12.
- [39] Wagner JM, Kremer TR, Van Dillen LR, Naismith RT. Plantarflexor weakness negatively impacts walking in persons with multiple sclerosis more than plantarflexor spasticity. *Archives of physical medicine and rehabilitation*. 2014;95:1358-65.
- [40] Maki BE. Gait changes in older adults: predictors of falls or indicators of fear. *Journal of American Geriatric Society*. 1997;45:313-20.



- [41] Hausdorff JM, Edelberg HK, Mitchell SL, Goldberger AL, Wei JY. Increased gait unsteadiness in community-dwelling elderly fallers. *Archives of physical medicine and rehabilitation*. 1997;78:278-83.
- [42] Socie MJ, Sosnoff JJ. Gait variability and multiple sclerosis. *Multiple Sclerosis International*. 2013.
- [43] Hof AL. The 'extrapolated center of mass' concept suggests a simple control of balance in walking. *Human movement science*. 2008;27:112-25.
- [44] Hof AL, van Bockel RM, Schoppen T, Postema K. Control of lateral balance in walking. Experimental findings in normal subjects and above-knee amputees. *Gait & posture*. 2007;25:250-8.
- [45] McAndrew Young PM, Wilken JM, Dingwell JB. Dynamic margins of stability during human walking in destabilizing environments. *Journal of biomechanics*. 2012;45:1053-9.
- [46] McAndrew Young PM, Dingwell JB. Voluntary changes in step width and step length during human walking affect dynamic margins of stability. *Gait & posture*. 2012;36:219-24.
- [47] Hak L, Houdijk H, Beek PJ, van Dieën JH. Steps to take to enhance gait stability: the effect of stride frequency, stride length, and walking speed on local dynamic stability and margins of stability. *PloS one*. 2013;8:e82842.
- [48] Kao PC, Dingwell JB, Higginson JS, Binder-Macleod S. Dynamic instability during post-stroke hemiparetic walking. *Gait & posture*. 2014;40:457-63.
- [49] Hak L, Houdijk H, van der Wurff P, Prins MR, Mert A, Beek PJ, et al. Stepping strategies used by post-stroke individuals to maintain margins of stability during walking. *Clinical biomechanics*. 2013;28:1041-8.
- [50] Hak L, van Dieën JH, van der Wurff P, Prins MR, Mert A, Beek PJ, et al. Walking in an unstable environment: strategies used by transtibial amputees to prevent falling during gait. *Archives of physical medicine and rehabilitation*. 2013;94:2186-93.
- [51] Dean JC, Kautz SA. Foot placement control and gait instability among people with stroke. *J Rehabil Res Dev*. 2015;52:577-90.
- [52] Zissimopoulos A, Stine R, Fatone S, Gard S. Mediolateral foot placement ability during ambulation in individuals with chronic post-stroke hemiplegia. *Gait & posture*. 2014;39:1097-102.
- [53] Hof AL, Vermerris SM, Gjaltema WA. Balance responses to lateral perturbations in human treadmill walking. *Journal of Exp Biol*. 2010;213:2655-64.
- [54] Hurt CP, Rosenblatt N, Crenshaw JR, Grabiner MD. Variation in trunk kinematics influences variation in step width during treadmill walking by older and younger adults. *Gait & posture*. 2010;31:461-4.
- [55] Wang Y, Srinivasan M. Stepping in the direction of the fall: the next foot placement can be predicted from current upper body state in steady-state walking. *Biology letters*. 2014;10.
- [56] Rankin BL, Buffo SK, Dean JC. A neuromechanical strategy for mediolateral foot placement in walking humans. *Journal of neurophysiology*. 2014;112:374-83.
- [57] Gates DH, Scott SJ, Wilken JM, Dingwell JB. Frontal plane dynamic margins of stability in individuals with and without transtibial amputation walking on a loose rock surface. *Gait & posture*. 2013;38:570-5.
- [58] Arvin M, Mazaheri M, Hoozemans MJ, Pijnappels M, Burger BJ, Verschueren SM, et al. Effects of narrow base gait on mediolateral balance control in young and older adults. *Journal of biomechanics*. 2016;49:1264-7.
- [59] Lockhart TE, Liu J. Differentiating fall-prone and healthy adults using local dynamic stability. *Ergonomics*. 2008;51:1860-72.
- [60] Toebes MJP, Hoozemans MJM, Furrer R, Dekker J, van Dieën JH. Local dynamic stability and variability of gait are associated with fall history in elderly subjects. *Gait & posture*. 2012;36:527-31.
- [61] van Schooten KS, Pijnappels M, Rispens SM, Elders PJ, Lips P, van Dieën JH. Ambulatory fall-risk assessment: amount and quality of daily-life gait predict falls in older adults. *The journals of gerontology Series A, Biological sciences and medical sciences*. 2015;70:608-15.
- [62] Spain RI, St George RJ, Salarian A, Mancini M, Wagner JM, Horak FB, et al. Body-worn motion sensors detect balance and gait deficits in people with multiple sclerosis who have normal walking speed. *Gait & posture*. 2012;35:573-8.

- [63] Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ. Principles of Neural Science (5th ed). New York: McGraw-Hill; 2012.
- [64] Moe-Nilssen R, Helbostad J. Trunk accelerometry as a measure of balance control during quiet standing. *Gait and Posture*. 2002;16:60-8.
- [65] Huisinga JM, Yentes JM, Filipi ML, Stergiou N. Postural control strategy during standing is altered in patients with multiple sclerosis. *Neuroscience letters*. 2012;524:124-8.
- [66] Kavanagh JJ, Menz HB. Accelerometry: a technique for quantifying movement patterns during walking. *Gait & posture*. 2008;28:1-15.
- [67] Mizuike C, Ohgi S, Morita S. Analysis of stroke patient walking dynamics using a tri-axial accelerometer. *Gait & posture*. 2009;30:60-4.
- [68] Vaillancourt DE, Newell KM. Changing complexity in human behavior and physiology through aging and disease. *Neurobiology of aging* 2002;23:1-11.
- [69] England SA, Granata KP. The influence of gait speed on local dynamic stability of walking. *Gait & posture*. 2007;25:172-8.
- [70] Bruijn SM, Meijer OG, Beek PJ, van Dieen JH. Assessing the stability of human locomotion: a review of current measures. *Journal of the Royal Society, Interface / the Royal Society*. 2013;10:20120999.
- [71] Wolf A. Determining Lyapunov exponents from a time series. *Physica D: Nonlinear Phenomena*. 1985;16.3:285-317.
- [72] Rosenstein MT, Collins JJ, De Luca CJ. A practical method for calculating largest Lyapunov exponents from small data sets. *Physica D: Nonlinear Phenomena*. 1993;65.1-2:117-34.
- [73] Bruijn SM, Bregman DJ, Meijer OG, Beek PJ, van Dieen JH. Maximum Lyapunov exponents as predictors of global gait stability: a modelling approach. *Med Eng Phys*. 2012;34:428-36.
- [74] Yentes JM, Hunt N, Schmid KK, Kaipust JP, McGrath D, Stergiou N. The appropriate use of approximate entropy and sample entropy with short data sets. *Annals of biomedical engineering*. 2013;41:349-65.
- [75] Kaplan DT, Furman M, Pincus SM, Ryan SM, Lipsitz LA, Goldberger AL. Aging and the complexity of cardiovascular dynamics. *Biophys J*. 1991;59:945-9.
- [76] Costa M, Ghiran I, Peng CK, Nicholson-Weller A, Goldberger AL. Complex dynamics of human red blood cell flickering: alterations with in vivo aging. *Physical review E, Statistical, nonlinear, and soft matter physics*. 2008;78:020901.
- [77] Cattaneo D, Carpinella I, Aprile I, Prosperini L, Montesano A, Jonsdottir J. Comparison of upright balance in stroke, Parkinson and multiple sclerosis. *Acta neurologica Scandinavica*. 2016;133:346-54.
- [78] Craig JJ, Bruetsch A, Huisinga JM. Relationship between trunk and foot accelerations during walking in healthy adults. *Gait & posture*. 2016;49:25-9.
- [79] Pavol MJ, Owings TM, Foley KT, Grabiner MD. Mechanisms Leading to a Fall From an Induced Trip in Healthy Older Adults. *Journal of Gerontology*. 2001;Vol. 56A:M428–M37.
- [80] van den Bogert AJ, Pavol MJ, Grabiner MD. Response time is more important than walking speed for the ability of older adults to avoid a fall after a trip. *Journal of biomechanics*. 2002;35:199-205.
- [81] Nagano H, Begg RK, Sparrow WA, Taylor S. Ageing and limb dominance effects on foot-ground clearance during treadmill and overground walking. *Clinical biomechanics*. 2011;26:962-8.
- [82] Mills PM, Barrett RS, Morrison S. Toe clearance variability during walking in young and elderly men. *Gait & posture*. 2008;28:101-7.
- [83] Santhiranayagam BK, Lai DT, Sparrow WA, Begg RK. Minimum toe clearance events in divided attention treadmill walking in older and young adults: a cross-sectional study. *Journal of neuroengineering and rehabilitation*. 2015;12:58.
- [84] Cameron MH, Horak FB, Herndon RR, Bourdette D. Imbalance in multiple sclerosis: a result of slowed spinal somatosensory conduction. *Somatosensory & motor research*. 2008;25:113-22.

- [85] Hess CW, Mills KR, Murray NM, Schrieffer TN. Magnetic brain stimulation: central motor conduction studies in multiple sclerosis. *Annals of neurology*. 1987;22:744-52.
- [86] Inglis JT, Kennedy PM, Wells C, Chua R. The role of cutaneous receptors in the foot. *US2002*.
- [87] Menz HB, Lord SR, St George R, Fitzpatrick RC. Walking stability and sensorimotor function in older people with diabetic peripheral neuropathy. *Archives of physical medicine and rehabilitation*. 2004;85:245-52.
- [88] Newsome SD, Wang JI, Kang JY, Calabresi PA, Zackowski KM. Quantitative measures detect sensory and motor impairments in multiple sclerosis. *Journal of the neurological sciences*. 2011;305:103-11.
- [89] Uszynski M, Purtill H, Coote S. Relationship between foot vibration threshold and walking and balance functions in people with Multiple Sclerosis (PwMS). *Gait & posture*. 2015;41:228-32.
- [90] Lambert CP, Archer RL, Evans WJ. Muscle strength and fatigue during isokinetic exercise in individuals with multiple sclerosis. *Medicine and science in sports and exercise*. 2001;33:1613-9.
- [91] Ng AV, Miller RG, Gelinas D, Kent-Braun JA. Functional relationships of central and peripheral muscle alterations in multiple sclerosis. *Muscle & nerve*. 2004;29:843-52.
- [92] Davies BL, Hoffman RM, Healey K, Zabad R, Kurz MJ. Errors in the ankle plantarflexor force production are related to the gait deficits of individuals with multiple sclerosis. *Human Movement Sciences*. 2017;51:91-8.
- [93] Rizzo MA, Hadjimichael OC, Preiningerova J, Vollmer TL. Prevalence and treatment of spasticity reported by multiple sclerosis patients. *multiple sclerosis*. 2004;10:589-95.
- [94] Hausdorff JM, Rios DA, Edelberg HK. Gait variability and fall risk in community-living older adults: a 1-year prospective study. *Archives of physical medicine and rehabilitation*. 2001;82:1050-6.
- [95] Riva F, Bisi MC, Stagni R. Gait variability and stability measures: minimum number of strides and within-session reliability. *Computers in biology and medicine*. 2014;50:9-13.
- [96] Zeni JA, Jr., Richards JG, Higginson JS. Two simple methods for determining gait events during treadmill and overground walking using kinematic data. *Gait & posture*. 2008;27:710-4.
- [97] van Schooten KS, Rispens SM, Pijnappels M, Daffertshofer A, van Dieen JH. Assessing gait stability: the influence of state space reconstruction on inter- and intra-day reliability of local dynamic stability during over-ground walking. *Journal of biomechanics*. 2013;46:137-41.
- [98] Richman JS, Moorman JR. Physiological time-series analysis using approximate entropy and sample entropy. *American Journal of Physiology-Heart and Circulatory Physiology*. 2000;278:2039-49.
- [99] Patterson KK, Gage WH, Brooks D, Black SE, McIlroy WE. Evaluation of gait symmetry after stroke: a comparison of current methods and recommendations for standardization. *Gait & posture*. 2010;31:241-6.
- [100] Moe-Nilssen R. A new method for evaluating motor control in gait under real-life environmental conditions. Part 2: Gait analysis. *Clin Biomech* 1998;13:328-35.
- [101] Bauby CE, Kuo AD. Active control of lateral balance in human walking. *Journal of biomechanics*. 2000;33.
- [102] Brach JS, Studenski S, Perera S, VanSwearingen JM, Newman AB. Stance time and step width variability have unique contributing impairments in older persons. *Gait & posture*. 2008;27:431-9.
- [103] Weerdesteyn V, de Niet M, van Duijnhoven HJ, Geurts AC. Falls in individuals with stroke. *Journal of rehabilitation research and development*. 2008;45:1195.
- [104] Fonteyn EM, Heeren A, Engels JJ, Boer JJ, van de Warrenburg BP, Weerdesteyn V. Gait adaptability training improves obstacle avoidance and dynamic stability in patients with cerebellar degeneration. *Gait & posture*. 2014;40:247-51.
- [105] Nyberg E, Broadway J, Finetto C, Dean J. A novel elastic force-field to influence mediolateral foot placement during walking. *IEEE transactions on neural systems and rehabilitation engineering : a publication of the IEEE Engineering in Medicine and Biology Society*. 2016.

- [106] Cattaneo D, Jonsdottir J, Zocchi M, Regola A. Effects of balance exercises on people with multiple sclerosis: a pilot study. *Clinical rehabilitation*. 2007;21:771-81.
- [107] Kasser SL, Jacobs JV, Ford M, Tourville TW. Effects of balance-specific exercises on balance, physical activity and quality of life in adults with multiple sclerosis: a pilot investigation. *Disability and rehabilitation*. 2015;37:2238-49.
- [108] Dingwell JB, Cusumano JP, Cavanagh PR, Sternad D. Local Dynamic Stability Versus Kinematic Variability of Continuous Overground and Treadmill Walking. *Journal of biomechanical engineering*. 2001;123:27.
- [109] Rispens SM, van Schooten KS, Pijnappels M, Daffertshofer A, Beek PJ, van Dieen JH. Identification of fall risk predictors in daily life measurements: gait characteristics' reliability and association with self-reported fall history. *Neurorehabilitation and neural repair*. 2015;29:54-61.
- [110] Winter D. Human balance and posture control during standing and walking. 1995.
- [111] Peebles AT, bruetsch A, Lynch SG, Huisinga JM. Dynamic balance in persons with multiple sclerosis who have a falls history is altered compared to non-fallers and to healthy controls. Under Review. 2017.
- [112] Callisaya ML, Blizzard L, McGinley JL, Schmidt MD, Srikanth VK. Sensorimotor Factors Affecting Gait Variability in Older People--A Population-Based Study. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*. 2009;65A:386-92.
- [113] Kurtzke J. Rating neurologic impairment in multiple sclerosis: An expanded disability status scale (EDSS). *Neurology*. 1983;33.11:1444-.
- [114] Horak FB, Macpherson JM. Postural orientation and equilibrium. *Comprehensive Physiology*. 2011:255-92.
- [115] Dingwell JB, Kang HG. Differences between local and orbital dynamic stability during human walking. *Journal of biomechanical engineering*. 2007;129:586-93.
- [116] Manor B, Wolenski P, Guevaro A, Li L. Differential effects of plantar desensitization on locomotion dynamics. *Journal of electromyography and kinesiology : official journal of the International Society of Electrophysiological Kinesiology*. 2009;19:e320-8.
- [117] Bell-Krotoski JA, Buford WL. The force/time relationship of clinically used sensory testing instruments. *Journal of Hand Therapy*. 1997;10:297-309.
- [118] Hoang PD, Cameron MH, Gandevia SC, Lord SR. Neuropsychological, balance, and mobility risk factors for falls in people with multiple sclerosis: a prospective cohort study. *Archives of physical medicine and rehabilitation*. 2014;95:480-6.
- [119] Morton SM, Bastian AJ. Cerebellar control of balance and locomotion. *The Neuroscientist : a review journal bringing neurobiology, neurology and psychiatry*. 2004;10:247-59.
- [120] Hoogkamer W, Bruijn SM, Sunaert S, Swinnen SP, Van Calenbergh F, Duysens J. Toward new sensitive measures to evaluate gait stability in focal cerebellar lesion patients. *Gait & posture*. 2015;41:592-6.
- [121] Franz JR, Maletis M, Kram R. Real-time feedback enhances forward propulsion during walking in old adults. *Clinical biomechanics*. 2014;29:68-74.
- [122] Jonsdottir J, Cattaneo D, Recalcati M, Regola A, Rabuffetti M, Ferrarin M, et al. Task-oriented biofeedback to improve gait in individuals with chronic stroke: motor learning approach. *Neurorehabilitation and neural repair*. 2010;24:478-85.
- [123] Dozza M, Horak FB, Chiari L. Auditory biofeedback substitutes for loss of sensory information in maintaining stance. *Experimental brain research*. 2007;178:37-48.
- [124] Begg RK, Tirosh O, Said CM, Sparrow WA, Steinberg N, Levinger P, et al. Gait training with real-time augmented toe-ground clearance information decreases tripping risk in older adults and a person with chronic stroke. *Frontiers in human neuroscience*. 2014;8:243.

- [125] Zackowski KM, Smith SA, Reich DS, Gordon-Lipkin E, Chodkowski BA, Sambandan DR, et al. Sensorimotor dysfunction in multiple sclerosis and column-specific magnetization transfer-imaging abnormalities in the spinal cord. *Brain*. 2009.
- [126] Michel L, Larochelle C, Prat A. Update on treatments in multiple sclerosis. *Presse medicale*. 2015;44:e137-51.
- [127] Maurer C, Peterka RJ. A new interpretation of spontaneous sway measures based on a simple model of human postural control. *Journal of neurophysiology*. 2005;93:189-200.

## Appendix

### Recruitment documents:

Volunteers are needed to serve as healthy controls subjects in a study examining walking and balance in persons with multiple sclerosis. Male and female volunteers between the ages of 20 and 60 years of age are needed. Volunteers should be free from any lower extremity orthopedic problem such as arthritis or ligament/tendon injuries (i.e. ACL injuries or meniscus tears) and free from any neurological or vestibular problems. This is a one-visit study that will last approximately 2-3 hours and you will be compensated for your time. We will measure your walking and balance using a three dimensional motion capture system. There is no invasive testing involved, i.e. no blood draws or similar tests. To see if you qualify for this study, contact Sara Kurtz at [skurtz@kumc.edu](mailto:skurtz@kumc.edu). In your inquiry, please indicate your age and sex.

PI for this study is Jessie Huisinga, PhD  
HSC approval number 13495

Subject Name (First, Last):

Sex:

Ethnicity:

Address:

Phone Number:

Email:

1. What is your age?

2. When were you diagnosed with MS?

3. Are you currently taking Ampyra or Dalfampridine?

☐

Yes\*

☐

No

4. Have you had any recent symptom exacerbations? If yes, then when approximately?

5. Do you feel like you have walking and balancing problems?

☐

Yes

☐

No

6. Do you wear an orthotic inside or outside? AFO?

- a. How often do you use the AFO and can you walk without it?

☐

I can walk without it.

☐

I cannot walk without it.\*

- b. Do you walk with a cane/walker always or only in public?

☐

Always

☐

Only in public

- c. Can you walk 25 feet without any kind of support?

☐

Yes

☐

No\*

7. Do you have any sort of orthopedic problem? Arthritis, joint replacements or pins in the body?

8. Do you have any vestibular problems? Any inner ear or balance disorders?

☐

Yes\*

☐

No

9. Are you diabetic?

☐

Yes\*

☐

No

\*Circle one:    Type I    Type II

\*Have you ever been diagnosed with diabetic neuropathy?

☐

Yes\*

☐

No

10. Are you color blind?

☐

Yes

☐

No

11. Do you have any significant vision problems?

☐

Yes

☐

No



# Kurtzke's Expanded Disability Status Scale Functional Systems Scoring:

## NEUROSTATUS SCORING

Scoring Sheet for a standardised, quantified neurological examination and assessment of Kurtzke's Functional Systems and Expanded Disability Status Scale in Multiple Sclerosis

STUDY NAME

### PERSONAL INFORMATION

Patient	
Date of Birth (04-Jun-1980)	- - - - - - - - - -
Centre Nr/Country	
Name of EDSS rater	
Date of Examination	- - - - - 2 0 - - - - -

### SYNOPSIS OF FS SCORES

1. Visual <sup>1</sup>		5. Sensory	
2. Brainstem		6. Bowel/Bladder <sup>1</sup>	
3. Pyramidal		7. Cerebral	
4. Cerebellar			

<sup>1</sup> = converted FS Score

EDSS Step

Signature

### 1. VISUAL (OPTIC) FUNCTIONS

OPTIC FUNCTIONS	OD	OS
Visual acuity (corrected)		
Visual fields		

Scotoma		
* Disc pallor		
FUNCTIONAL SYSTEM SCORE		

### 2. BRAINSTEM FUNCTIONS

CRANIAL NERVE EXAMINATION	
Extraocular movements (EOM) impairment	
Nystagmus	
Trigeminal damage	
Facial weakness	

Hearing loss	
Dysarthria	
Dysphagia	
Other cranial nerve functions	
FUNCTIONAL SYSTEM SCORE	

### 3. PYRAMIDAL FUNCTIONS

REFLEXES	R	> <	L
Biceps			
Triceps			
Brachioradialis			
Knee			
Ankle			
Plantar response			
Cutaneous reflexes			
* Palmomental reflex			

Knee flexors		
Knee extensors		
Plantar flexion (feet/toes)		
Dorsiflexion (feet/toes)		
* Position test UE, pronation		
* Position test UE, downward drift		
* Position test LE, sinking		
Able to lift only one leg at a time (grade in °)		
* Walking on heels		
* Walking on toes		
* Hopping on one foot		

LIMB STRENGTH	R	L
Deltoids		
Biceps		
Triceps		
Wrist/finger flexors		
Wrist/finger extensors		
Hip flexors		

SPASTICITY		
Arms		
Legs		
Gait		
FUNCTIONAL SYSTEM SCORE		

\* = optional  
<sup>1</sup> = converted FS Score

#### 4. CEREBELLAR FUNCTIONS

##### CEREBELLAR EXAMINATION

Head tremor	
Truncal ataxia	
	R L
Tremor/dysmetria UE	
Tremor/dysmetria LE	

Rapid alternating movements UE impairment	
Rapid alternating movements LE impairment	
Tandem walking	
Gait ataxia	
Romberg test	
Other, e. g. rebound	
FUNCTIONAL SYSTEM SCORE	

#### 5. SENSORY FUNCTIONS

##### SENSORY EXAMINATION

	R L
Superficial sensation UE	
Superficial sensation trunk	
Superficial sensation LE	
Vibration sense UE	
Vibration sense LE	

Position sense UE	
Position sense LE	
* Lhermitte's sign	
* Paraesthesiae UE	
* Paraesthesiae trunk	
* Paraesthesiae LE	
FUNCTIONAL SYSTEM SCORE	

#### 6. BOWEL/ BLADDER FUNCTIONS

Urinary hesitancy/retention	
Urinary urgency/incontinence	
Bladder catheterisation	

Bowel dysfunction	
* Sexual dysfunction	
FUNCTIONAL SYSTEM SCORE	

#### 7. CEREBRAL FUNCTIONS

##### MENTAL STATUS EXAMINATION

+ Depression	
+ Euphoria	

Decrease in mentation	
* Fatigue	
FUNCTIONAL SYSTEM SCORE	

#### 8. AMBULATION

Walking range as reported (without help or sticks)

meters	
in min	
Distance able to walk without rest or assistance	
≥ 100 meters, but < 200 meters	
≥ 200 meters, but < 300 meters	
≥ 300 meters, but < 500 meters	
≥ 500 meters but not unrestricted	
Unrestricted	
Actual distance (obligatory up to 500 m if possible)	
meters	

Requires <b>constant</b> assistance to walk 100 meters	
Unilateral assistance (in meters)	
Cane/crutch	
Other	
Bilateral assistance (in meters)	
Canes/crutches	
Other	
Assistance by another person (in meters)	

\* = optional

<sup>1</sup> = converted FS Score

\* Because depression, euphoria and fatigue are difficult to evaluate objectively, in some studies it does not contribute to the Cerebral FS score or EDSS step. Please adhere to the study's specific instructions.

Standardised Neurological Examination and Assessment of Kurtzke's Functional Systems and Expanded Disability Status Scale  
Slightly modified from J.F. Kurtzke, Neurology 1983;33,1444-52

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**Appendix Table 1: Raw data - foot motion for healthy controls**

Subject	Leg	Step Width		Step Length		Stride Time		Minimum Toe Clearance	
		Average (cm)	CV (%)	Average (cm)	CV (%)	Average (s)	CV (%)	Average (cm)	SD (%)
1	Left	10.13	27.27	43.17	8.47	1.14	3.72	1.53	4.26
1	Right	10.61	29.60	39.22	7.47	1.14	3.77	1.26	3.79
2	Left	5.75	37.96	53.70	1.81	1.28	1.32	0.92	1.74
2	Right	8.51	25.32	51.59	2.46	1.28	1.40	1.17	2.37
3	Left	5.50	26.04	49.89	3.30	1.13	1.60	1.24	2.55
3	Right	5.91	24.58	53.83	3.16	1.13	1.72	1.15	2.55
4	Left	7.75	32.60	55.58	5.87	1.07	1.47	0.95	2.66
4	Right	15.30	12.97	55.50	3.18	1.07	1.41	0.27	2.45
5	Left	8.17	23.90	44.59	6.01	1.74	4.21	0.54	2.29
5	Right	11.86	17.00	48.47	5.29	1.74	3.94	0.52	2.47
6	Left	3.29	75.21	54.42	2.75	1.24	1.55	2.06	3.49
6	Right	7.37	30.67	50.17	2.98	1.24	1.56	1.57	3.45
7	Left	15.52	14.79	50.90	2.70	1.19	1.64	1.68	2.46
7	Right	16.76	14.73	51.83	3.22	1.19	1.79	1.78	2.41
8	Left	7.21	23.87	51.90	2.89	1.24	1.66	1.13	3.06
8	Right	10.61	13.55	49.41	3.23	1.24	1.74	1.01	2.64
9	Left	5.77	22.86	32.21	5.69	1.31	2.27	2.80	3.83
9	Right	7.08	15.04	28.18	6.40	1.31	2.23	2.90	3.99
10	Left	6.50	26.33	52.33	2.36	1.08	1.57	1.15	2.70
10	Right	9.74	15.77	52.26	2.25	1.08	1.53	0.88	2.86
11	Left	2.22	87.40	65.89	1.87	1.39	1.32	1.35	3.33
11	Right	2.58	75.59	64.25	2.04	1.39	1.51	1.75	3.20
12	Left	9.00	19.03	44.07	2.00	1.19	1.42	1.07	1.84
12	Right	6.73	21.70	46.76	2.33	1.19	1.37	0.85	2.28
13	Left	9.72	26.74	51.85	3.71	1.56	2.86	1.11	3.37
13	Right	10.86	21.18	51.30	3.95	1.56	3.09	0.89	3.39
14	Left	12.49	14.14	35.77	8.19	1.29	4.83	1.47	5.37
14	Right	14.00	11.39	36.22	6.84	1.29	4.76	1.42	3.88
15	Left	12.20	13.22	34.34	7.05	1.25	3.46	1.97	2.31
15	Right	14.15	12.89	38.85	6.44	1.25	3.60	1.16	3.53
16	Left	10.78	22.66	51.74	3.18	0.93	1.91	1.08	4.38
16	Right	9.37	23.96	51.16	3.11	0.93	1.95	1.32	3.82
17	Left	12.92	19.68	37.21	6.79	1.30	4.50	1.73	4.23
17	Right	11.85	19.50	37.13	7.37	1.30	4.52	11.23	3.55
18	Left	7.33	10.61	59.93	1.63	1.14	1.30	-0.08	2.33
18	Right	9.17	9.21	57.30	1.55	1.14	1.31	0.26	2.48

19	Left	6.29	43.22	68.05	2.04	1.11	1.28	1.55	2.67
19	Right	8.40	34.26	68.93	1.93	1.11	1.31	0.91	2.59
20	Left	8.42	19.87	28.47	7.12	1.09	3.38	32.35	3.79
20	Right	9.26	19.78	29.84	5.75	1.09	3.31	39.42	4.31
21	Left	4.47	38.16	34.98	12.08	1.26	12.33	24.69	6.19
21	Right	5.55	30.72	35.54	14.50	1.26	12.19	22.35	5.61
22	Left	5.16	21.00	41.37	3.30	1.16	2.36	0.31	1.62
22	Right	5.07	23.28	44.65	3.17	1.16	2.51	0.24	1.55
23	Left	13.27	21.75	44.98	6.14	1.44	3.33	0.61	2.29
23	Right	15.24	19.15	44.56	4.96	1.44	3.09	0.88	3.09
24	Left	14.01	10.49	59.74	1.76	1.09	1.29	0.80	2.73
24	Right	13.46	11.21	63.51	1.55	1.09	1.35	0.58	2.07
25	Left	7.79	29.26	68.18	1.88	1.13	1.26	1.91	2.84
25	Right	10.46	23.13	71.08	1.45	1.13	1.36	1.12	2.20
26	Left	10.50	27.47	75.53	1.56	0.98	1.34	1.68	3.25
26	Right	10.42	27.85	73.72	1.99	0.98	1.41	1.63	2.60
27	Left	11.10	19.51	71.55	1.94	1.11	1.50	0.88	3.37
27	Right	11.57	18.04	73.31	2.20	1.11	1.49	0.21	1.84

**Appendix Table 2: Raw data - foot motion for non-fallers with MS**

Subject	Leg	Step Width		Step Length		Stride Time		Minimum Toe Clearance	
		Average (cm)	CV (%)	Average (cm)	CV (%)	Average (s)	CV (%)	Average (cm)	SD (%)
1	Left	4.88	37.14	47.10	3.40	1.30	2.83	0.06	1.65
1	Right	8.25	22.17	49.53	3.48	1.30	2.90	0.49	2.29
2	Left	18.60	14.57	31.16	7.99	1.50	4.71	17.45	4.01
2	Right	19.09	10.52	29.11	9.35	1.50	4.65	1.56	3.06
3	Left	16.27	15.56	52.80	3.20	1.19	1.77	0.40	2.29
3	Right	12.26	23.36	55.58	3.46	1.19	1.84	0.87	2.05
4	Left	4.98	31.71	26.38	7.82	1.78	4.08	0.92	2.39
4	Right	6.29	20.93	24.05	9.83	1.78	4.08	1.08	2.13
5	Left	3.88	47.45	49.73	6.52	1.65	3.82	1.02	3.78
5	Right	2.72	57.30	46.50	8.03	1.65	3.74	0.86	3.41
6	Left	6.65	41.17	46.44	5.17	1.26	3.38	1.02	3.09
6	Right	7.38	27.67	46.40	4.99	1.26	3.44	0.74	2.88
7	Left	8.28	16.51	42.30	4.72	1.29	2.61	0.82	3.15
7	Right	8.77	13.35	40.22	4.39	1.29	2.75	1.38	3.30
8	Left	4.93	49.46	57.06	2.55	1.21	1.93	1.33	3.19
8	Right	8.64	31.77	52.05	3.45	1.21	1.65	0.58	2.89

<b>9</b>	Left	12.57	19.07	33.74	9.37	1.46	5.68	1.47	3.40
<b>9</b>	Right	12.84	16.27	38.15	8.33	1.46	5.74	1.31	3.83
<b>10</b>	Left	12.36	14.54	39.24	7.87	1.40	7.40	1.31	3.07
<b>10</b>	Right	11.12	13.13	30.62	10.36	1.40	7.59	1.51	5.19
<b>11</b>	Left	8.80	20.52	51.75	2.67	1.38	2.15	0.32	1.90
<b>11</b>	Right	11.46	15.43	51.01	2.67	1.38	2.13	2.58	2.08
<b>12</b>	Left	11.45	21.00	51.19	3.95	1.33	2.08	2.70	4.17
<b>12</b>	Right	13.24	18.04	50.26	4.80	1.33	1.94	2.45	3.71
<b>13</b>	Left	9.98	29.34	46.68	4.30	1.15	2.59	1.17	2.19
<b>13</b>	Right	8.78	29.45	49.18	3.47	1.15	2.82	1.36	4.50
<b>14</b>	Left	11.10	24.95	43.58	5.33	1.35	3.48	0.93	2.38
<b>14</b>	Right	12.16	19.38	49.55	3.52	1.35	3.90	0.73	2.20
<b>15</b>	Left	7.56	38.45	39.06	5.16	1.38	3.31	0.24	1.71
<b>15</b>	Right	10.09	26.46	39.08	5.50	1.38	3.53	0.27	1.61
<b>16</b>	Left	17.41	17.93	37.91	9.79	1.79	6.57	0.92	3.23
<b>16</b>	Right	17.33	18.63	36.87	10.98	1.79	7.45	0.63	1.84
<b>17</b>	Left	11.47	15.36	40.73	5.90	1.30	4.24	0.75	2.44
<b>17</b>	Right	9.75	17.35	36.66	8.92	1.31	4.14	0.96	3.52
<b>18</b>	Left	4.42	109.87	41.47	7.61	1.32	4.93	1.41	5.55
<b>18</b>	Right	5.74	73.03	42.43	8.42	1.32	4.88	1.88	4.90
<b>19</b>	Left	9.12	15.05	52.02	2.71	1.13	1.91	0.89	2.76
<b>19</b>	Right	9.68	14.71	54.21	3.41	1.13	1.80	1.56	3.04
<b>20</b>	Left	10.09	19.66	37.07	5.25	1.31	3.23	1.47	2.41
<b>20</b>	Right	10.65	19.99	43.85	5.43	1.31	3.33	2.14	4.94
<b>21</b>	Left	10.88	15.79	63.75	1.86	1.19	1.20	3.87	5.66
<b>21</b>	Right	10.40	13.99	63.23	1.99	1.19	1.27	3.22	4.48
<b>22</b>	Left	15.46	15.83	56.68	3.29	1.12	1.94	1.56	3.59
<b>22</b>	Right	15.88	16.29	56.43	2.34	1.12	2.13	1.36	2.88
<b>23</b>	Left	12.80	17.92	47.15	3.03	1.14	1.72	0.95	2.36
<b>23</b>	Right	11.44	20.44	51.09	2.67	1.14	1.78	1.30	2.09
<b>24</b>	Left	5.69	27.38	54.37	5.58	1.48	5.37	0.94	4.62
<b>24</b>	Right	4.87	35.64	54.18	5.80	1.48	5.49	0.91	3.94
<b>25</b>	Left	11.12	25.46	42.54	4.38	1.15	2.66	0.76	3.15
<b>25</b>	Right	12.06	24.48	44.49	4.07	1.15	2.62	1.22	3.30
<b>26</b>	Left	8.88	30.99	53.97	2.77	1.27	1.42	1.20	1.74
<b>26</b>	Right	9.39	28.84	53.90	2.78	1.27	1.60	0.42	2.67
<b>27</b>	Left	10.67	33.76	50.84	4.46	1.49	2.37	0.93	2.73
<b>27</b>	Right	10.54	36.05	54.28	3.52	1.49	2.71	0.48	2.63
<b>28</b>	Left	6.14	20.77	20.07	14.70	1.68	7.30		
<b>28</b>	Right	6.11	21.36	11.32	22.27	1.68	7.31		

**Appendix Table 3: Raw data - foot motion for fallers with MS**

Subject	Leg	Step Width		Step Length		Stride Time		Minimum Toe Clearance	
		Average (cm)	CV (%)	Average (cm)	CV (%)	Average (s)	CV (%)	Average (cm)	SD (%)
1	Left	1.03	150.59	21.91	12.57	1.67	7.94		
1	Right	1.87	80.63	17.65	17.39	1.67	8.38		
2	Left	9.19	17.67	43.23	4.87	1.55	2.15	0.87	2.58
2	Right	10.89	15.36	43.78	4.74	1.55	2.10	1.16	3.20
3	Left	3.97	71.46	42.08	3.74	1.98	4.39	0.53	2.26
3	Right	6.03	39.26	41.06	6.90	1.98	4.10	-0.10	2.16
4	Left	10.61	7.65	14.10	12.98	1.77	4.82		
4	Right	11.87	6.30	19.36	12.45	1.77	4.68		
5	Left	13.15	13.77	27.34	11.79	1.37	8.18		
5	Right	12.24	17.46	26.03	16.13	1.37	8.32		
6	Left	23.23	9.10	18.22	17.81	1.37	6.31		
6	Right	22.83	8.85	19.84	14.92	1.37	6.19		
7	Left	12.71	13.64	34.70	7.71	2.03	4.09	2.27	2.87
7	Right	12.30	14.50	33.24	7.18	2.03	4.15	0.96	3.41
8	Left	12.89	25.72	32.17	16.01	1.71	10.59	1.15	6.82
8	Right	13.15	21.74	33.02	17.16	1.71	10.45	3.48	6.03
9	Left	9.57	20.40	33.37	10.56	1.66	4.41		
9	Right	7.48	24.75	25.42	14.83	1.66	4.30		
10	Left	6.89	18.62	38.49	9.74	1.54	4.25	0.23	3.55
10	Right	5.23	25.31	33.55	10.75	1.54	4.65	0.68	3.33
11	Left	4.80	79.00	66.81	2.24	1.07	2.00	1.15	3.76
11	Right	4.69	71.76	63.48	3.64	1.07	2.06	1.03	3.94
12	Left	10.27	33.13	52.21	3.60	1.60	2.37	1.63	2.15
12	Right	8.28	46.35	53.19	4.54	1.60	2.34	1.80	2.39
13	Left	9.87	23.84	51.13	4.90	1.19	3.67	0.55	3.10
13	Right	8.92	28.35	52.32	3.93	1.19	3.70	0.57	2.78
14	Left	11.67	20.97	39.86	11.88	2.00	8.06	0.75	3.01
14	Right	8.76	28.60	44.12	7.31	2.00	8.04	0.20	2.55
15	Left	7.62	23.50	32.88	17.00	1.71	21.38		
15	Right	5.50	35.53	23.38	30.00	1.71	21.01		
16	Left	13.36	16.22	32.60	5.55	1.61	4.02	0.92	1.98
16	Right	12.86	18.28	35.07	6.35	1.61	3.74	0.83	2.77
17	Left	15.82	14.26	31.91	10.54	1.51	4.03	0.97	3.18
17	Right	14.78	20.57	34.42	10.20	1.51	4.98	2.88	7.05
18	Left	4.42	34.32	29.22	8.92	2.07	7.51	0.41	1.92
18	Right	5.67	25.42	29.52	9.92	2.07	7.73	0.38	2.43

19	Left	10.64	7.00	54.33	2.23	1.40	1.44	0.90	2.79
19	Right	9.60	7.25	58.99	1.99	1.40	1.34	0.86	3.06
20	Left								
20	Right								
21	Left	3.05	127.78	55.08	4.56	1.07	2.83	1.74	3.81
21	Right	3.38	129.07	55.97	4.67	1.07	2.73	0.87	4.35
22	Left	17.16	9.80	9.22	22.74	1.03	6.17		
22	Right	17.21	11.94	5.27	39.70	1.03	5.83		
23	Left	7.92	14.83	50.39	3.69	1.29	2.60	0.77	3.22
23	Right	6.86	15.65	50.27	3.35	1.29	2.51	0.92	3.19
24	Left	9.21	13.67	23.02	10.44	2.32	6.88	5.37	6.69
24	Right	9.24	13.74	25.62	10.43	2.32	6.89	0.80	4.68
25	Left	5.33	29.65	23.20	10.76	1.63	2.69	0.89	3.08
25	Right	6.22	25.93	23.50	9.05	1.63	3.77	0.83	2.79
26	Left	18.00	16.03	18.50	20.57	1.60	6.66		
26	Right	18.94	14.43	17.59	18.82	1.60	6.60		
27	Left	12.79	19.43	33.48	5.81	1.60	3.99	0.84	2.82
27	Right	12.66	19.95	32.91	6.87	1.60	3.66	0.87	2.94

**Appendix Table 4: Raw data – trunk accelerations for healthy controls**

Subject	RMS			Lyapunov Exponents			Sample Entropy		
	AP	ML	VT	AP	ML	VT	AP	ML	VT
1	1.16	1.24	1.68	0.0502	0.0131	0.0171	1.67	1.56	1.24
2	0.74	0.76	0.89	0.0411	0.0327	0.0305	1.74	1.71	1.66
3									
4	1.01	1.46	1.60	0.0234	0.0123	0.0118	1.78	1.38	1.32
5	0.87	0.71	1.16	0.0210	0.0117	0.0132	1.26	1.60	1.15
6	0.46	0.42	0.77	0.0393	0.0263	0.0342	1.90	2.01	1.35
7	0.66	0.92	1.30	0.0419	0.0268	0.0472	1.98	1.98	1.47
8	0.70	0.81	1.44	0.0195	0.0119	0.0128	1.32	1.32	0.73
9	0.75	0.88	1.18	0.0304	0.0156	0.0179	1.74	1.39	1.35
10	1.06	0.82	1.45	0.0426	0.0177	0.0155	1.66	1.92	1.20
11	1.03	0.68	1.67	0.0136	0.0134	0.0111	1.35	1.52	0.84
12	1.06	0.76	1.43	0.0238	0.0111	0.0133	1.39	1.53	0.97
13	0.44	0.53	0.89	0.0222	0.0174	0.0209	1.92	1.66	1.28
14	0.55	0.76	0.80	0.0257	0.0173	0.0305	1.98	1.65	1.58
15	0.95	0.92	1.03	0.0271	0.0180	0.0226	1.87	1.71	1.57
16	1.76	1.50	3.05	0.0301	0.0417	0.0131	1.85	1.86	1.10
17	0.63	1.14	0.90	0.0483	0.0173	0.0202	2.02	1.24	1.75
18	0.92	0.85	1.59	0.0276	0.0113	0.0087	1.28	1.21	0.79
19	1.47	1.13	2.27	0.0210	0.0100	0.0106	1.10	1.43	0.79



20	0.97	0.72	1.07	0.0760	0.0246	0.0278	2.06	1.59	1.63
21	0.49	0.78	0.82	0.0428	0.0246	0.0395	1.96	1.37	1.75
22	0.81	0.94	1.42	0.0272	0.0151	0.0167	1.76	1.78	1.18
23	0.71	0.99	1.01	0.0545	0.0250	0.0325	2.03	1.72	1.56
24	1.46	1.07	2.05	0.0145	0.0112	0.0103	1.33	1.58	0.83
25	1.31	1.21	2.42	0.0165	0.0088	0.0103	1.53	1.39	0.80
26	1.53	1.49	3.60	0.0302	0.0179	0.0137	1.46	1.56	0.78
27	1.42	1.30	2.51	0.0236	0.0124	0.0139	1.42	1.48	0.81

**Appendix Table 5: Raw data – trunk accelerations for non-fallers with MS**

subject	RMS			Lyapunov Exponents			Sample Entropy		
	AP	ML	VT	AP	ML	VT	AP	ML	VT
1	1.47	0.63	1.00	0.0459	0.0133	0.0217	1.63	1.67	1.38
2	0.59	0.94	0.72	0.0364	0.0145	0.0306	1.89	1.36	1.95
3	1.08	1.13	1.44	0.0140	0.0108	0.0106	1.31	1.08	1.05
4	0.33	0.48	0.31	0.0358	0.0465	0.0555	2.00	1.80	2.01
5	0.63	0.52	0.68	0.0288	0.0242	0.0263	1.78	1.89	1.88
6	0.88	0.77	1.25	0.0302	0.0166	0.0204	1.75	1.74	1.28
7	0.45	0.89	0.99	0.0123	0.0217	0.0275	1.84	1.79	1.29
8	0.96	0.84	1.54	0.0222	0.0257	0.0108	1.71	2.00	1.09
9	0.73	1.02	0.76	0.0260	0.0163	0.0279	1.97	1.31	1.94
10	0.87	0.68	0.93	0.0248	0.0422	0.0250	1.94	1.93	1.47
11	0.59	0.50	0.89	0.0199	0.0172	0.0165	1.51	1.73	1.27
12	0.77	0.92	1.08	0.0275	0.0155	0.0195	1.44	1.28	1.33
13	0.99	0.91	1.60	0.0282	0.0189	0.0250	1.69	1.69	1.18
14	0.76	0.63	0.98	0.0672	0.0186	0.0194	1.81	1.69	1.29
15	0.66	0.74	0.86	0.0236	0.0123	0.0251	1.86	1.50	1.54
16	0.67	1.02	0.59	0.0317	0.0178	0.0292	1.86	1.20	1.89
17	0.66	0.56	0.83	0.0238	0.0161	0.0181	1.98	1.81	1.69
18	0.96	1.11	1.15	0.0540	0.0246	0.0204	2.06	1.61	1.69
19	0.51	0.79	1.46	0.0298	0.0199	0.0189	1.95	1.48	1.20
20	0.69	0.97	0.85	0.0681	0.0193	0.0213	1.93	1.34	1.69
21	1.02	0.83	2.10	0.0135	0.0116	0.0093	1.32	1.26	0.73
22	1.16	1.15	1.73	0.0269	0.0109	0.0171	1.68	1.42	1.15
23	1.03	1.09	1.45	0.0181	0.0113	0.0142	1.60	1.49	1.14
24	1.10	0.54	0.81	0.0218	0.0473	0.0228	1.63	2.05	1.80
25	0.91	1.42	1.00	0.0205	0.0098	0.0166	1.51	1.04	1.48
26	0.89	0.99	1.23	0.0175	0.0117	0.0114	1.54	1.38	0.98
27	0.62	0.77	1.32	0.0225	0.0420	0.0250	1.88	1.71	1.23
28	0.51	0.38	0.58	0.0325	0.0484	0.0343	1.74	1.96	1.82



**Appendix Table 6: Raw data – trunk accelerations for fallers with MS**

subject	RMS			Lyapunov Exponents			Sample Entropy		
	AP	ML	VT	AP	ML	VT	AP	ML	VT
1	1.34	0.57	0.40	0.0232	0.0203	0.0251	1.27	1.55	2.02
2	0.74	0.57	0.83	0.0171	0.0311	0.0198	1.73	1.94	1.77
3	0.50	0.61	0.50	0.0215	0.0189	0.0169	1.59	1.15	1.68
4	0.49	0.25	0.21	0.0144	0.0274	0.0311	1.72	2.00	1.99
5	1.33	0.81	0.83	0.0304	0.0326	0.0313	1.84	1.73	1.81
6	0.48	1.25	0.51	0.0306	0.0145	0.0227	1.91	0.92	1.87
7	0.69	0.65	0.41	0.0269	0.0174	0.0287	1.57	1.39	1.93
8	0.88	0.64	0.53	0.0272	0.0363	0.0342	1.55	1.85	1.97
9	0.73	0.77	0.67	0.0616	0.0428	0.0273	2.07	1.93	2.04
10	0.95	0.53	0.74	0.0223	0.0284	0.0213	1.61	1.78	1.77
11	1.38	1.17	2.48	0.0226	0.0166	0.0141	1.58	1.75	1.09
12	0.83	0.66	1.26	0.0220	0.0150	0.0216	1.54	1.56	1.27
13	0.97	0.81	1.37	0.0288	0.0518	0.0236	1.85	2.00	1.58
14	0.81	0.34	0.34	0.0195	0.0649	0.0298	1.49	2.00	1.69
15	0.50	0.40	0.39	0.0318	0.0512	0.0401	1.96	1.78	1.96
16	0.64	1.10	0.74	0.0280	0.0139	0.0161	1.84	1.08	1.73
17	0.74	1.38	0.87	0.0220	0.0189	0.0182	1.76	1.18	1.72
18	0.45	0.27	0.29	0.0255	0.0440	0.0293	1.58	1.81	1.71
19	0.87	0.55	0.75	0.0188	0.0113	0.0145	1.88	1.77	1.41
20	0.80	0.41	0.60	0.0175	0.0140	0.0143	1.69	1.79	1.50
21	0.82	1.18	1.90	0.0277	0.0207	0.0196	1.79	1.80	1.32
22	0.65	0.75	0.87	0.0445	0.0493	0.0324	1.96	1.84	1.73
23	0.84	0.69	0.97	0.0255	0.0469	0.0243	1.78	1.96	1.64
24	1.02	0.60	0.60	0.0206	0.0194	0.0193	1.06	1.27	1.37
25	0.37	0.45	0.46	0.0290	0.0195	0.0222	1.94	1.78	1.91
26	0.44	0.88	0.46	0.0399	0.0231	0.0346	1.90	1.17	1.94
27	0.63	0.73	0.52	0.0430	0.0147	0.0195	1.71	1.33	1.89

**Appendix Table 7: Raw data – margin of stability for healthy controls**

Subject	Leg	Mediolateral Margin of Stability			Anterior-posterior Margin of Stability		
		Average (cm)	CV (%)	Asymmetry (%)	Average (cm)	CV (%)	Asymmetry (%)
1	Left	11.79	12.05	4.23	30.10	7.78	3.60
1	Right	12.30	10.38		29.04	7.22	
2	Left	13.48	7.54	10.76	43.06	2.48	0.56
2	Right	15.01	5.89		43.30	2.65	

3	Left	14.93	5.78	2.57	36.54	3.65	6.36
3	Right	14.55	6.82		38.94	3.30	
4	Left	11.17	9.55	32.66	42.07	9.84	0.53
4	Right	15.53	6.93		42.29	2.63	
5	Left	15.70	9.14	7.19	38.91	4.31	2.17
5	Right	16.87	8.63		39.77	3.80	
6	Left	15.86	6.77	20.09	45.21	2.70	2.03
6	Right	19.40	5.84		44.30	2.79	
7	Left	15.39	8.34	11.78	37.72	3.31	0.94
7	Right	17.32	7.09		38.07	2.99	
8	Left	13.50	6.83	28.57	40.51	2.24	0.33
8	Right	18.00	4.51		40.38	1.95	
9	Left	12.00	6.98	7.77	25.97	5.44	4.58
9	Right	12.97	6.02		24.80	6.38	
10	Left	11.66	8.51	15.65	39.84	2.57	0.90
10	Right	13.64	6.29		39.48	2.19	
11	Left	12.66	9.07	5.08	48.30	1.74	2.84
11	Right	13.32	9.54		46.95	1.92	
12	Left	17.74	4.82	11.16	38.74	1.92	1.97
12	Right	15.87	5.82		39.52	1.59	
13	Left	14.23	12.52	1.19	42.80	2.82	3.94
13	Right	14.40	9.90		44.52	3.27	
14	Left	16.18	6.88	13.57	33.20	5.16	2.01
14	Right	14.12	7.13		32.54	4.44	
15	Left	15.24	7.72	1.37	29.75	5.20	10.74
15	Right	15.03	8.51		33.13	4.74	
16	Left	15.58	6.92	22.62	36.12	3.61	1.27
16	Right	12.42	9.65		36.58	3.58	
17	Left	15.84	7.24	14.48	34.96	4.48	8.58
17	Right	13.70	9.30		38.09	4.60	
18	Left	14.36	4.66	5.97	43.75	1.42	2.64
18	Right	13.52	4.79		42.61	1.44	
19	Left	15.72	7.79	1.38	51.20	1.52	1.21
19	Right	15.94	8.27		50.59	1.50	
20	Left	15.85	6.17	25.28	26.77	7.52	4.17
20	Right	12.30	8.38		25.68	6.38	
21	Left	21.07	6.43	9.24	34.81	9.27	2.18
21	Right	19.21	11.14		35.58	11.00	
22	Left	12.21	7.32	5.06	37.36	2.71	2.47
22	Right	12.85	7.46		38.29	2.05	
23	Left	14.31	11.05	5.26	37.01	4.59	1.38
23	Right	15.08	9.74		37.52	4.31	

<b>24</b>	Left	14.24	5.29	14.75	44.66	2.01	2.68
<b>24</b>	Right	12.29	5.91		45.87	1.93	
<b>25</b>	Left	15.21	7.71	5.51	50.81	1.85	2.61
<b>25</b>	Right	14.39	8.30		52.15	1.59	
<b>26</b>	Left	15.72	8.98	26.02	49.92	2.47	8.01
<b>26</b>	Right	12.10	12.57		54.08	4.23	
<b>27</b>	Left	16.39	6.50	8.40	50.07	2.07	3.57
<b>27</b>	Right	15.07	6.24		51.89	2.02	

**Appendix Table 8: Raw data – margin of stability for non-fallers with MS**

Subject	Leg	Mediolateral Margin of Stability			Anterior-posterior Margin of Stability		
		Average (cm)	CV (%)	Asymmetry (%)	Average (cm)	CV (%)	Asymmetry (%)
<b>1</b>	Left	18.37	5.76	5.54	37.46	3.13	3.52
<b>1</b>	Right	19.41	4.46		38.80	3.59	
<b>2</b>	Left	18.98	8.88	1.48	32.03	8.62	6.14
<b>2</b>	Right	18.70	6.07		30.12	7.22	
<b>3</b>	Left	24.17	5.15	24.32	43.88	2.59	2.21
<b>3</b>	Right	18.93	7.16		44.87	1.95	
<b>4</b>	Left	12.18	8.78	2.91	25.31	7.81	2.37
<b>4</b>	Right	11.83	7.76		24.71	9.18	
<b>5</b>	Left	16.12	9.20	1.15	39.19	7.73	2.65
<b>5</b>	Right	15.93	9.31		38.17	7.01	
<b>6</b>	Left	13.24	7.28	17.72	36.71	3.95	2.35
<b>6</b>	Right	15.82	6.66		35.85	3.81	
<b>7</b>	Left	13.86	7.63	4.89	35.44	4.40	1.40
<b>7</b>	Right	14.55	6.50		35.94	4.00	
<b>8</b>	Left	12.04	11.12	26.13	45.67	2.52	6.57
<b>8</b>	Right	15.66	8.84		42.76	2.31	
<b>9</b>	Left	21.86	8.99	9.12	31.69	10.39	7.89
<b>9</b>	Right	19.95	7.54		34.30	7.43	
<b>10</b>	Left	21.02	6.26	40.78	30.51	7.37	25.92
<b>10</b>	Right	13.90	10.64		23.51	9.33	
<b>11</b>	Left	14.36	6.26	2.64	43.02	2.38	2.36
<b>11</b>	Right	13.99	7.31		44.05	2.31	
<b>12</b>	Left	19.33	6.13	9.48	41.67	3.41	2.86
<b>12</b>	Right	17.58	7.02		40.49	3.85	
<b>13</b>	Left	16.53	8.58	12.89	38.32	3.47	2.74
<b>13</b>	Right	14.53	8.94		39.39	3.03	

14	Left	14.67	7.84	2.28	42.33	4.41	5.84
14	Right	15.01	8.97		44.88	2.63	
15	Left	18.65	10.34	10.60	35.47	4.96	9.49
15	Right	16.77	6.63		32.25	5.03	
16	Left	19.11	12.42	32.25	35.48	10.68	3.62
16	Right	26.46	7.94		34.22	10.44	
17	Left	14.99	8.89	5.08	34.74	5.25	1.43
17	Right	14.24	7.54		34.24	7.19	
18	Left	15.73	14.60	20.27	38.27	6.08	7.64
18	Right	12.84	16.18		35.45	5.20	
19	Left	17.18	5.02	4.98	41.07	2.72	4.30
19	Right	16.35	5.76		42.88	2.96	
20	Left	19.88	5.87	3.71	34.18	3.92	9.63
20	Right	19.15	7.10		37.64	3.99	
21	Left	13.98	6.82	24.52	46.82	1.83	0.96
21	Right	10.92	7.47		46.37	2.18	
22	Left	16.98	7.91	10.79	43.01	3.34	2.49
22	Right	15.24	7.21		41.96	3.12	
23	Left	15.18	6.47	20.99	37.85	2.53	3.51
23	Right	12.30	8.76		39.20	2.13	
24	Left	14.83	9.43	32.72	40.94	5.57	4.34
24	Right	10.66	16.60		39.20	6.00	
25	Left	17.81	7.17	16.17	38.24	2.48	5.15
25	Right	15.15	8.55		36.32	2.56	
26	Left	17.52	6.72	12.18	42.34	2.42	6.04
26	Right	15.50	10.33		44.98	2.06	
27	Left	18.56	10.34	20.12	47.32	4.01	4.82
27	Right	15.17	13.83		49.66	3.01	
28	Left	16.84	6.88	26.57	14.35	15.93	21.84
28	Right	12.89	9.30		11.53	21.77	

**Appendix Table 9: Raw data – margin of stability for fallers with MS**

Subject	Leg	Mediolateral Margin of Stability			Anterior-posterior Margin of Stability		
		Average (cm)	CV (%)	Asymmetry (%)	Average (cm)	CV (%)	Asymmetry (%)
1	Left	15.42	10.71	16.84	13.70	30.08	28.47
1	Right	18.26	9.95		10.28	43.98	

<b>2</b>	Left	16.86	9.57	5.11	34.70	4.74	0.37
<b>2</b>	Right	16.02	9.93		34.57	5.56	
<b>3</b>	Left	20.64	10.11	18.84	44.90	4.03	3.07
<b>3</b>	Right	24.93	8.13		43.54	4.22	
<b>4</b>	Left	12.97	4.46	8.33	7.08	31.14	29.73
<b>4</b>	Right	14.09	4.69		9.56	20.06	
<b>5</b>	Left	15.31	10.24	19.64	16.74	13.98	13.20
<b>5</b>	Right	12.57	14.73		19.10	14.62	
<b>6</b>	Left	16.87	9.00	4.99	18.69	9.51	2.47
<b>6</b>	Right	16.05	9.77		19.16	11.20	
<b>7</b>	Left	16.15	9.46	14.34	30.47	6.73	5.32
<b>7</b>	Right	13.99	13.72		32.13	6.40	
<b>8</b>	Left	25.00	12.00	33.08	31.00	14.54	3.65
<b>8</b>	Right	17.90	17.57		32.15	15.24	
<b>9</b>	Left	15.51	8.70	19.89	21.79	13.87	17.98
<b>9</b>	Right	12.70	10.06		18.19	17.27	
<b>10</b>	Left	20.59	8.89	71.13	28.76	12.85	6.43
<b>10</b>	Right	9.78	18.46		26.97	14.60	
<b>11</b>	Left	16.22	8.98	0.24	50.30	3.53	0.81
<b>11</b>	Right	16.25	8.86		49.89	3.93	
<b>12</b>	Left	12.93	12.40	11.78	44.87	2.42	2.28
<b>12</b>	Right	11.49	14.90		45.90	2.87	
<b>13</b>	Left	13.24	13.90	4.06	40.57	3.97	4.02
<b>13</b>	Right	12.71	11.43		38.97	4.09	
<b>14</b>	Left	18.82	11.34	31.49	32.01	10.90	4.97
<b>14</b>	Right	13.70	17.44		33.64	7.07	
<b>15</b>	Left	17.11	10.38	22.87	18.59	36.38	64.34

<b>15</b>	Right	13.60	12.32		9.54	72.69	
<b>16</b>	Left	21.91	6.06	12.45	33.89	4.88	3.49
<b>16</b>	Right	19.34	6.30		35.09	5.57	
<b>17</b>	Left	17.75	8.21	26.05	34.80	6.52	7.38
<b>17</b>	Right	13.66	16.39		37.46	5.21	
<b>18</b>	Left	12.49	9.94	3.38	21.08	12.00	0.54
<b>18</b>	Right	12.08	8.99		21.20	11.94	
<b>19</b>	Left	17.38	3.77	6.29	41.98	2.61	3.91
<b>19</b>	Right	16.32	3.17		43.66	2.16	
<b>20</b>	Left						
<b>20</b>	Right						
<b>21</b>	Left	14.82	13.67	21.88	41.09	5.63	3.39
<b>21</b>	Right	11.90	18.58		42.50	5.36	
<b>22</b>	Left	17.82	9.98	25.31	12.75	13.78	5.22
<b>22</b>	Right	13.81	11.36		12.10	15.83	
<b>23</b>	Left	15.91	6.09	23.61	40.79	5.35	0.15
<b>23</b>	Right	12.55	7.44		40.85	4.05	
<b>24</b>	Left	16.36	7.00	32.58	14.68	26.85	4.51
<b>24</b>	Right	11.77	13.52		15.36	30.61	
<b>25</b>	Left	15.71	6.63	1.24	25.20	9.46	3.88
<b>25</b>	Right	15.51	7.56		24.24	6.18	
<b>26</b>	Left	21.43	9.33	24.05	23.85	12.91	2.36
<b>26</b>	Right	16.83	11.88		23.29	12.37	
<b>27</b>	Left	22.48	6.84	22.67	30.59	5.65	1.06
<b>27</b>	Right	17.91	8.38		30.92	4.81	

**Appendix Table 10: Raw data – Physiological impairments for non-fallers with MS**

subject	Vibration Threshold	Spasticity	Sensorimotor Delays	EDSS Pyramidal	EDSS Cerebellar	EDSS Sensory
1	2.50	0.67	111.3	1	1	1
2	1.15	0.00	175.8	2	1	1
3	5.10	0.00	120.2			
4	7.75	1.00	126.1	2	2	2
5	4.40	0.00	129.3	0	1	1
6	3.25	0.33	82.8	2	0	1
7	3.20	0.67	124.1	0	0	2
8	2.35	0.67	122.7	0	0	1
9	4.85	0.67	120.6	0	0	1
10	4.40	0.00	123.7	0	0	0
11	4.10	0.33	116.6	0	0	0
12	10.50	0.00	144.7	1	3	1
13	1.55	0.00	118.7	0	0	0
14	2.80	0.00	90.9	0	0	1
15	4.50	1.33	117.7	0	0	2
16	1.45	0.00	138.3	1	0	0
17	2.45	0.00	95.8	2	0	2
18	5.95	0.33	227.8	3	0	2
19	3.95	0.33	94.7	1	0	0
20	9.80	1.33	136.3	2	1	3
21	2.45	0.00	126.6	1	0	0
22	2.90	0.00	118.5			
23	2.70	0.67	100.7	1	0	0
24	2.65	0.33	100.3	1	0	0
25	2.35	0.33	85.3			
26	3.10	0.33	114.3	1	1	0
27	1.70	0.67	116.0	1	0	0
28	1.65	0.00	100.0	1	0	0

**Appendix Table 10: Raw data – Physiological impairments for fallers with MS**

subject	Vibration Threshold	Spasticity	Sensorimotor Delays	EDSS Pyramidal	EDSS Cerebellar	EDSS Sensory
1	5.50	1.00	148.7	1	2	0
2	9	3.33	163.7	2	1	3
3	3.75	0.67	143.2	2	0	3
4	4.05	0.33	120.1	1	0	0
5	8.00	2.00	176.7	2	4	
6	2.90	0.33	146.4	1	0	0

<b>7</b>	10.90	0.00	153.4	2	3	3
<b>8</b>	9.05	0.67	168.8	3	3	3
<b>9</b>	3.35	1.33	95.5	1	2	0
<b>10</b>	2.15	0.00	214.7	3	0	1
<b>11</b>	2.40	0.67	163.7	0	2	2
<b>12</b>	8.40	0.33	123.6	1	1	1
<b>13</b>	5.35	0.33	125.4	2	0	2
<b>14</b>	3.90	1.00	121.3	2	2	0
<b>15</b>	11.55	0.00	219.2	3	3	3
<b>16</b>	6.80	0.67	117.0	2	1	1
<b>17</b>	6.95	0.67	154.9	2	3	1
<b>18</b>	10.00	0.67	159.6	2	3	3
<b>19</b>	7.60		246.7	2	3	
<b>20</b>	8.50	1.67	141.1	2	2	2
<b>21</b>	10.35	1.00	207.0	2	1	2
<b>22</b>	3.60	0.00	129.4	2	0	1
<b>23</b>	1.45	0.00	100.7	0	0	0
<b>24</b>	3.50	0.33	123.3	0	0	0
<b>25</b>	11.85	2.33	130.7	3	2	1
<b>26</b>	2.50	0.33	101.3	1	0	0
<b>27</b>	5.45	1.67	98.2	2	0	0



## MATLAB code used:

Code used to process motion capture data and calculate spatiotemporal parameters and margin of stability for each subject:

```
clear;
%basis: (1=x=AP) (2=y=ML) (3=z)

keepgraphs = 0; % 1 to keep 0 to close all. If batch run, close all plots
filtneeded = 0; % 1 yes 0 no.

group = ['controls'];
file =
{'MSC03';'MSC04';'MSC05';'MSC11';'MSC13';'MSC14';'MSC15';'MSC17';'MSC18';'MSC21';'MSC24';'MSC26';'M
SC29';'MSC31';'MSC32';'MSC34';'MSC35';'MSC37';'MSC38';'MSC40';'MSC42';'MSC43';'MSC47';'MSC48';'MSC4
9';'MSC50';'MSC51'};

% group = ['nonfallers'];
% file =
{'MS05';'MS09';'MS13';'MS16';'MS17';'MS18';'MS23';'MS26';'MS29';'MS31';'MS32';'MS44';'MS45';'MS47';'MS48';
'MS49';'MS50';'MS60';'MS69';'MS71';'MS78';'MS81';'MS82';'MS84';'MS85';'MS89';'MS105';'MS112'};

% group = ['fallers'];
% file =
{'MS12';'MS14';'MS21';'MS30';'MS33';'MS36';'MS37';'MS56';'MS57';'MS59';'MS61';'MS66';'MS67';'MS76';'MS91';
'MS95';'MS97';'MS100';'MS108';'MS110';'MS111';'MS113';'MS119';'MS121';'MS122';'MS124'};

for subject = 1:length(file(:,1))
%% This first block loads the data from the 3 minute trial, and assigns a name (ie RHeel(AP,ML,VT)) for each
marker

clearvars -except file group subject keepgraphs filtneeded

if length(group) == 8 %are you running the control group or an MS group?
    A = dlmread(['S:\coa\motion_analysis_data\MS study\controls\' char(file{subject,:}) '\Trimmed\Trimmed_'
char(file{subject,:}) 'C5_t1.trc'],",6,2);
else
    A = dlmread(['S:\coa\motion_analysis_data\MS study\ms subjects\' char(file{subject,:}) '\Trimmed\Trimmed_'
char(file{subject,:}) 'C5_t1.trc'],",6,2);
end
srate = length(A)/180;
t_mk = [1/srate:1/srate:(length(A(:,1))/1/srate)];
clear M;
k=1;%counter
j=1;%basis vector
n=1;%marker number
%for n=1:
for i=1:75%take off troch
    if k>3
        k=1;
        n=n+1;
    end
    M(:,k,n) = A(:,i);
    if k<=3
```

```

    k=k+1;
end
end

%This while loop just names each marker from its number
while 1
RASIS = M(:,1);
RPSIS = M(:,2);
LASIS = M(:,3);
LPSIS = M(:,4);
VSacral = M(:,5);
RTroch = M(:,6);
%Rmidthigh = M(:,7);
RThigh = M(:,7);
RKnee = M(:,8);
RShank = M(:,9);
Rlowershank = M(:,10);
RAnkle = M(:,11);
RToe = M(:,12);
RHeel = M(:,13);
RMTPlat = M(:,14);
Rcallat = M(:,15);
LTroch = M(:,16);
%Lmidthigh = M(:,17);
LThigh = M(:,17);
LKnee = M(:,18);
LShank = M(:,19);
Llowershank = M(:,20);
LAnkle = M(:,21);
LToe = M(:,22);
LHeel = M(:,23);
LMTPlat = M(:,24);
Lcallat = M(:,25);
break;
end

%% This block calculates the Center of Mass (Whittle, M. W. Human Movement Science 16.2 347-355, (1997).)
for i=1:length(t_mk)
    for k=1:3
        COM(i,k) = (((LPSIS(i,k)+RPSIS(i,k))/2)+LASIS(i,k)+RASIS(i,k))/3;
    end
end

%% This block identifies heel strike time indicies, and filters heel marker trajectories if heel marker trajectory
% is noisy and heel strikes are poorly identified (you need to identify if
% this happens by looking at the output plots

if filtneeded == 1
%Design the 4th order digital low pass filter with a cutoff frequency of 10 Hz
order = 4; %fourth order filter
nyquist_frequency = sr/2; %compute the nyquist frequency
cutoff_LP = 6; %cutoff frequency in Hz
normalized_cutoff = cutoff_LP/nyquist_frequency;

[b,a] = butter(order, normalized_cutoff , 'low');
%b and a are now my filter coefficients

```

```

%use filtfilt to do a forward and backward pass, using reflected data to
%minimize startup transients
LH_F = filtfilt(b,a,LHeel(:,1));
RH_F = filtfilt(b,a,RHeel(:,1));
end

R_heel = RH_F*-1;
[pks,R_HS] = findpeaks(R_heel,'MinPeakDistance',20);

L_heel(:,1) = LH_F*-1;
[pks,L_HS] = findpeaks(L_heel,'MinPeakDistance',20);

%% here the 3 minute trial is broken up into 4 time periods and plotted. The
%%used needs to look at these plots to assure that heel strikes were
%%correctly identified

% 0-45 45-90 90-135 135-180
LMax = max(max(LToe(:,3)),max(LHeel(:,3)))+20;
RMax = max(max(RToe(:,3)),max(RHeel(:,3)))+20;
LMin = min(LToe(:,3))-15;
RMin = min(RToe(:,3))-15;
savefigurefolder = ['S:\coa\hpl\alex\Thesis Analysis\MoS\' group \' char(file{subject,:})];

figure(1);

subplot(2,1,1)
plot(t_mk,LHeel(:,3),'b');
title(['Left Heel' file(subject,:)])
xlabel('AP')
ylabel('Verticle Axis')
axis([0 45 (LMin-10) LMax])
hold on
for i=1:length(L_HS)
    text(t_mk(L_HS(i))+0.2,LHeel(L_HS(i),3)+30,num2str(i),'FontSize',6);
    hold on
end
plot(t_mk(L_HS),LHeel(L_HS,3),'k*');
hold on

subplot(2,1,2)
plot(t_mk,RHeel(:,3),'b');
title('Right Heel')
xlabel('AP')
ylabel('Verticle Axis')
axis([0 45 RMin-10 RMax])
hold on
for i=1:length(R_HS)
    text(t_mk(R_HS(i))+0.2,RHeel(R_HS(i),3)+30,num2str(i),'FontSize',6);
    hold on
end
plot(t_mk(R_HS),RHeel(R_HS,3),'k*');

```

```

hold on

set(gcf,'units','normalized','outerposition',[0 0 1 1])

figurename = [savefigurefolder '_1.jpg'];
saveas(1,figurename)

figure(2);

subplot(2,1,1)
plot(t_mk,LHeel(:,3),'b');
title(['Left Heel' file(subject,:)])
xlabel('AP')
ylabel('Verticle Axis')
axis([45 90 (LMin-10) LMax])
hold on
for i=1:length(L_HS)
    text(t_mk(L_HS(i))+0.2,LHeel(L_HS(i),3)+30,num2str(i),'FontSize',6);
    hold on
end
plot(t_mk(L_HS),LHeel(L_HS,3),'k*');
hold on

subplot(2,1,2)
plot(t_mk,RHeel(:,3),'b');
title('Right Heel')
xlabel('AP')
ylabel('Verticle Axis')
axis([45 90 RMin-10 RMax])
hold on
for i=1:length(R_HS)
    text(t_mk(R_HS(i))+0.2,RHeel(R_HS(i),3)+30,num2str(i),'FontSize',6);
    hold on
end
plot(t_mk(R_HS),RHeel(R_HS,3),'k*');
hold on

set(gcf,'units','normalized','outerposition',[0 0 1 1])

figurename = [savefigurefolder '_2.jpg'];
saveas(2,figurename)

figure(3);

subplot(2,1,1)
plot(t_mk,LHeel(:,3),'b');
title(['Left Heel' file(subject,:)])
xlabel('AP')
ylabel('Verticle Axis')
axis([90 135 (LMin-10) LMax])
hold on
for i=1:length(L_HS)
    text(t_mk(L_HS(i))+0.2,LHeel(L_HS(i),3)+30,num2str(i),'FontSize',6);
    hold on
end
plot(t_mk(L_HS),LHeel(L_HS,3),'k*');

```

```

hold on

subplot(2,1,2)
plot(t_mk,RHeel(:,3),'b');
title('Right Heel')
xlabel('AP')
ylabel('Verticle Axis')
axis([90 135 RMin-10 RMax])
hold on
for i=1:length(R_HS)
    text(t_mk(R_HS(i))+0.2,RHeel(R_HS(i),3)+30,num2str(i),'FontSize',6);
    hold on
end
plot(t_mk(R_HS),RHeel(R_HS,3),'k*');
hold on

set(gcf,'units','normalized','outerposition',[0 0 1 1])

figurename = [savefigurefolder '_3.jpg'];
saveas(3,figurename)

figure(4);

subplot(2,1,1)
plot(t_mk,LHeel(:,3),'b');
title(['Left Heel' file(subject,:)])
xlabel('AP')
ylabel('Verticle Axis')
axis([135 180 (LMin-10) LMax])
hold on
for i=1:length(L_HS)
    text(t_mk(L_HS(i))+0.2,LHeel(L_HS(i),3)+30,num2str(i),'FontSize',6);
    hold on
end
plot(t_mk(L_HS),LHeel(L_HS,3),'k*');
hold on

subplot(2,1,2)
plot(t_mk,RHeel(:,3),'b');
title('Right Heel')
xlabel('AP')
ylabel('Verticle Axis')
axis([135 180 RMin-10 RMax])
hold on
for i=1:length(R_HS)
    text(t_mk(R_HS(i))+0.2,RHeel(R_HS(i),3)+30,num2str(i),'FontSize',6);
    hold on
end
plot(t_mk(R_HS),RHeel(R_HS,3),'k*');
hold on

set(gcf,'units','normalized','outerposition',[0 0 1 1])

figurename = [savefigurefolder '_4.jpg'];
saveas(4,figurename)

```

```

%% calculates leg length (CoM-Ankle) (McAndrew Young et al. Journal of biomechanics. 2012.)
%Caclulate Right Leg Length
McA_RLeg_Length = sqrt(((COM(:,1)-RAnkle(:,1)).^2) + ((COM(:,2) - RAnkle(:,2)).^2) + ((COM(:,1) -
RAnkle(:,1)).^2))/1000;
McA_Max_RLeg_Length = max(McA_RLeg_Length);

%Caclulate Left Leg Length
McA_LLeg_Length = sqrt(((COM(:,1)-LAnkle(:,1)).^2) + ((COM(:,2) - LAnkle(:,2)).^2) + ((COM(:,1) -
LAnkle(:,1)).^2))/1000;
McA_Max_LLeg_Length = max(McA_LLeg_Length);

%% This Block Calculates the Velocity of the CoM (Sacral) in the AP direction
vel_data_points_AP = length(COM(:,1)); %Figures out the total number sacral position points (frames)
vel_AP = zeros(vel_data_points_AP,1);

    for i = 1:(vel_data_points_AP) %loops over the total number of sacral points/positions using a first
order central difference equation when you have less than 4 points
        %if the number of data points is greater than
        %three a second order, forward central difference
        %equation was used to calculate
        %velocity at the first data point and a second order, backward
        %central difference equation was used to calculate
        % velocity at the last point and a first
        %order central difference quation is used for
        %every other data point
        if i>1 && i<vel_data_points_AP %calculating for eeverything but the first and last point
            vel_AP(i,1) = (((COM(i+1,1)-COM(i-1,1))/(2/60))/1000);
        elseif i == 1 %velocity for the first point
            vel_AP(i,1) = (((-3.*COM(i,1))+4.*COM(i+1,1)-(COM(i+2,1)))/(2/60))/1000);
        elseif i == vel_data_points_AP %velocity for the last point
            vel_AP(i,1) = (((3.*COM(i,1))-(4.*COM(i-1,1))+(COM(i-2,1)))/(2/60))/1000);
        end
    end

%% This Block Calculates the Velocity of the CoM (Sacral) in the ML direction
vel_data_points_ML = length(COM(:,2)); %Figures out the total number sacral position points (frames)
vel_ML = zeros(vel_data_points_ML,1);

    for i = 1:(vel_data_points_ML) %loops over the total number of sacral points/positions using a first
order central difference equation when you have less than 4 points
        %if the number of data points is greater than
        %three a second order, forward central difference
        %equation was used to calculate
        %velocity at the first data point and a second order, backward
        %central difference equation was used to calculate
        % velocity at the last point and a first
        %order central difference quation is used for
        %every other data point
        if i>1 && i<vel_data_points_ML %calculating for eeverything but the first and last point
            vel_ML(i,1) = (((COM(i+1,2)-COM(i-1,2))/(2/60))/1000);
        elseif i == 1 %velocity for the first point
            vel_ML(i,1) = (((-3.*COM(i,2))+4.*COM(i+1,2)-(COM(i+2,2)))/(2/60))/1000);
        elseif i == vel_data_points_ML %velocity for the last point
            vel_ML(i,1) = (((3.*COM(i,2))-(4.*COM(i-1,2))+(COM(i-2,2)))/(2/60))/1000);
        end
    end

```

```

%% This block calculates MoS at each right and left HS and plots them

R_xCoM_AP = COM(:,1)./1000 + (vel_AP./sqrt(9.81./McA_RLeg_Length));

for i=1:length(R_HS)
    R_AP_HS(i) = R_xCoM_AP(R_HS(i)) - RToe(R_HS(i),1)./1000;
end

figure(5)
subplot(2,1,2)
plot(1:length(R_HS),R_AP_HS)
set(gca,'XTick', 0:5:length(R_HS));
title(['Right Foot AP MoS at heel strike' file(subject,:)])
xlabel('Stride')
ylabel('MoS (m)')

L_xCoM_AP = COM(:,1)./1000 + (vel_AP./sqrt(9.81./McA_LLeg_Length));

for i=1:length(L_HS)
    L_AP_HS(i) = L_xCoM_AP(L_HS(i)) - LToe(L_HS(i),1)./1000;
end

subplot(2,1,1)
plot(1:length(L_HS),L_AP_HS)
set(gca,'XTick', 0:5:length(L_HS));
title('Left Foot AP MoS at heel strike')
xlabel('Stride')
ylabel('MoS (m)')
set(gcf,'units','normalized','outerposition',[0 0 1 1])
figurename = [savefigurefolder '_5.jpg'];
saveas(5,figurename)

%% This block calculates MoS at each right and left HS and plots them

R_xCoM_ML = COM(:,2)./1000 + (vel_ML./sqrt(9.81./McA_RLeg_Length));

for i=1:length(R_HS)
    R_ML_HS(i) = RMTPlat(R_HS(i),2)./1000 - R_xCoM_ML(R_HS(i));
end

figure(6)
subplot(2,1,2)
plot(1:length(R_ML_HS),R_ML_HS)
set(gca,'XTick', 0:5:length(R_HS));
legend('hs')
title(['Right Foot ML MoS' file(subject,:)])
xlabel('Stride')
ylabel('MoS (m)')

L_xCoM_ML = COM(:,2)./1000 + (vel_ML./sqrt(9.81./McA_LLeg_Length));

```

```

for i=1:length(L_HS)
L_ML_HS(i) = L_xCoM_ML(L_HS(i)) - LMTPlat(L_HS(i),2)./1000;
end

subplot(2,1,1)
plot(1:length(L_ML_HS),L_ML_HS)
set(gca,'XTick', 0:5:length(L_HS));
title('Left Foot ML MoS')
xlabel('Stride')
ylabel('MoS (m)')
set(gcf,'units','normalized','outerposition',[0 0 1 1])
figurename = [savefigurefolder '_6.jpg'];
saveas(6,figurename)

%% This block calculates step length and width at each HS, and stride time

for i=1:length(L_HS)
    L_SL(i) = abs(RHeel(L_HS(i),1) - LHeel(L_HS(i),1));
    L_SW(i) = RHeel(L_HS(i),2) - LHeel(L_HS(i),2);
end

for i=1:length(L_HS)-1
    L_ST(i) = (L_HS(i+1) - L_HS(i))/srate;
end

for i=1:length(R_HS)
    R_SL(i) = abs(LHeel(R_HS(i),1) - RHeel(R_HS(i),1));
    R_SW(i) = RHeel(R_HS(i),2) - LHeel(R_HS(i),2);
end

for i=1:length(R_HS)-1
    R_ST(i) = (R_HS(i+1) - R_HS(i))/srate;
end

LFirst = L_HS(1)<R_HS(1); % 1- left first, 0- right first

figure(7)
subplot(2,1,2)
plot(1:length(R_HS),(R_SL-mean(R_SL))/range(R_SL),1:length(R_HS),(R_SW-
mean(R_SW))/range(R_SW),1:length(R_ST),(R_ST-mean(R_ST))/range(R_ST))
set(gca,'XTick', 0:5:length(R_HS));
legend('SL','SW','ST')
title(['Right Foot stepping pattern' file(subject,:)])
xlabel('Stride')
ylabel('m')

subplot(2,1,1)
plot(1:length(L_HS),(L_SL-mean(L_SL))/range(L_SL),1:length(L_HS),(L_SW-
mean(L_SW))/range(L_SW),1:length(L_ST),(L_ST-mean(L_ST))/range(L_ST))
set(gca,'XTick', 0:5:length(L_HS));
legend('SL','SW','ST')
title('Left Foot stepping pattern')
xlabel('Stride')
ylabel('m')
set(gcf,'units','normalized','outerposition',[0 0 1 1])

```



```

figurename = [savefigurefolder '_7.jpg'];
saveas(7,figurename)

%% Collect all outcome variables and write them to an excel spreadsheet

outleft = [(1:length(L_HS))' L_ML_HS' L_AP_HS' L_SW' L_SL' [L_ST NaN]];
xlswrite(['S:\coa\hpl\alex\Thesis Analysis\MoS\' group '_results.xlsx'],outleft,char(file{subject,:}),['A3']);

pause(1)

outright = [(1:length(R_HS))' R_ML_HS' R_AP_HS' R_SW' R_SL' [R_ST NaN]];
xlswrite(['S:\coa\hpl\alex\Thesis Analysis\MoS\' group '_results.xlsx'],outright,char(file{subject,:}),['G3']);

pause(1)

xlswrite(['S:\coa\hpl\alex\Thesis Analysis\MoS\' group '_results.xlsx'],LFirst,char(file{subject,:}),['O2']);

if keepgraphs==0
close all
end
end

```

Code used to process motion capture data and calculate minimum toe clearance:

```

clear;
%basis: (1=x=AP) (2=y=ML) (3=z)
keepgraphs = 0; %0-no, 1=yes
filtneeded = 1;

% group = ['controls'];
% file =
{'MSC03';'MSC04';'MSC05';'MSC11';'MSC13';'MSC14';'MSC15';'MSC17';'MSC18';'MSC21';'MSC24';'MSC26';'M
SC29';'MSC31';'MSC32';'MSC34';'MSC35';'MSC37';'MSC38';'MSC40';'MSC42';'MSC43';'MSC47';'MSC48';'MSC4
9';'MSC50';'MSC51'};

% group = ['nonfallers'];
% file =
{'MS05';'MS09';'MS13';'MS16';'MS17';'MS18';'MS23';'MS26';'MS29';'MS31';'MS32';'MS44';'MS45';'MS47';'MS48';
'MS49';'MS50';'MS60';'MS69';'MS71';'MS78';'MS81';'MS82';'MS84';'MS85';'MS89';'MS105';'MS112'};

% group = ['fallers'];
% file =
{'MS12';'MS14';'MS21';'MS30';'MS33';'MS36';'MS37';'MS56';'MS57';'MS59';'MS61';'MS66';'MS67';'MS76';'MS91';
'MS95';'MS97';'MS100';'MS108';'MS110';'MS111';'MS113';'MS119';'MS121';'MS122';'MS124'};

group = ['controls'];
file = {'MSC07';'MSC09';'MSC20'};

for subject = 1:length(file(:,1))
%% This first block loads the data from the 3 minute trial, and assigns a name (ie RHeel(AP,ML,VT)) for each
marker

```

```
clearvars -except file group subject keepgraphs filtneeded
```

```
healthresh = 80;
```

```
if length(group) == 8
```

```
    A = dlmread(['S:\coa\motion_analysis_data\MS study\controls\' char(file{subject,:}) '\Trimmed\Trimmed_'  
char(file{subject,:}) 'C5_t1.trc'],",6,2);
```

```
else
```

```
    A = dlmread(['S:\coa\motion_analysis_data\MS study\ms subjects\' char(file{subject,:}) '\Trimmed\Trimmed_'  
char(file{subject,:}) 'C5_t1.trc'],",6,2);
```

```
end
```

```
srate = length(A)/180;
```

```
t_mk = [1/srate:1/srate:(length(A(:,1))/1/srate)];
```

```
clear M;
```

```
k=1;%counter
```

```
j=1;%basis vector
```

```
n=1;%marker number
```

```
%for n=1:
```

```
for i=1:75%take off troch
```

```
    if k>3
```

```
        k=1;
```

```
        n=n+1;
```

```
    end
```

```
    M(:,k,n) = A(:,i);
```

```
    if k<=3
```

```
        k=k+1;
```

```
    end
```

```
end
```

```
%This while loop just names each marker from its number
```

```
while 1
```

```
RASIS = M(:,1);
```

```
RPSIS = M(:,2);
```

```
LASIS = M(:,3);
```

```
LPSIS = M(:,4);
```

```
VSacral = M(:,5);
```

```
RTroch = M(:,6);
```

```
%Rmidthigh = M(:,7);
```

```
RThigh = M(:,7);
```

```
RKnee = M(:,8);
```

```
RShank = M(:,9);
```

```
Rlowershank = M(:,10);
```

```
RAnkle = M(:,11);
```

```
RToe = M(:,12);
```

```
RHeel = M(:,13);
```

```
RMTPlat = M(:,14);
```

```
Rcallat = M(:,15);
```

```
LTroch = M(:,16);
```

```
%Lmidthigh = M(:,17);
```

```
LThigh = M(:,17);
```

```
LKnee = M(:,18);
```

```
LShank = M(:,19);
```

```
Llowershank = M(:,20);
```

```

LAnkle = M(:,21);
LToe = M(:,22);
LHeel = M(:,23);
LMTPlat = M(:,24);
Lcallat = M(:,25);
break;
end

%% This block calculates the Center of Mass (Whittle, M. W. Human Movement Science 16.2 347-355, (1997).)
for i=1:length(t_mk)
    for k=1:3
        COM(i,k) = (((LPSIS(i,k)+RPSIS(i,k))/2)+LASIS(i,k)+RASIS(i,k))/3;
    end
end

%% This block identifies heel strike time indicies, and filters marker trajectories if they
%% are noisy and heel strikes or toe clearances are poorly identified (you need to identify if
%% this happens by looking at the output plots

if filtneeded == 1
    %Design the 4th order digital low pass filter with a cutoff frequency of 10 Hz
    order = 4; %fourth order filter
    nyquist_frequency = srates/2; %compute the nyquist frequency
    cutoff_LP = 6; %cutoff frequency in Hz
    normalized_cutoff = cutoff_LP/nyquist_frequency;

    [b,a] = butter(order, normalized_cutoff, 'low');
    %b and a are now my filter coefficients

    %use filtfilt to do a forward and backward pass, using reflected data to
    %minimize startup transients
    LH_F = filtfilt(b,a,LHeel(:,1));
    RH_F = filtfilt(b,a,RHeel(:,1));

    LT_AP = filtfilt(b,a,LToe(:,1));
    RT_AP = filtfilt(b,a,RToe(:,1));

    LT_VT = filtfilt(b,a,LToe(:,3));
    RT_VT = filtfilt(b,a,RToe(:,3));
end

%Find HS
R_heel = RH_F*-1;
[~,R_HS] = findpeaks(R_heel,'MinPeakDistance',40);

L_heel = LH_F*-1;
[~,L_HS] = findpeaks(L_heel,'MinPeakDistance',40);

%Find TO
[~,L_TO] = findpeaks(LT_AP,'MinPeakDistance',20);

[~,R_TO] = findpeaks(RT_AP,'MinPeakDistance',20);

%% Find Minimum toe clearance during swing phase. first find two peaks of toe

```

```

% trajectory, then minimum between the two. If only one peak then there
% will be no true local minimum. you then take the MTC as the toe height at
% the average %swing phase for other true MTC
l=1;
lm=1;
LTMax=[0 0];

if L_HS(1)<L_TO(1)
    L_HS = L_HS(2:end);
end

if L_TO(end)>L_HS(end)
    L_TO = L_TO(1:end-1);
end

for i=1:length(L_TO)
    [ltpeak ltpeakid] = findpeaks(LToe(L_TO(i):L_HS(i)+5,3),'MinPeakDistance',5);
    [lvalue lvalueID] = sort(ltpeak,'descend');
    if length(lvalueID)>1
        if ltpeakid(lvalueID(2))<ltpeakid(lvalueID(1)) %low peak first
            [Lmtc(l) LmtcID_nonadj(l)] =
min(LToe((L_TO(i)+ltpeakid(lvalueID(2))):(L_TO(i)+ltpeakid(lvalueID(1)))),3));
            LmtcID(l) = LmtcID_nonadj(l) + (L_TO(i)+ltpeakid(lvalueID(2)))-1;
            LSecondpeak(l,:) = [(L_TO(i)+ltpeakid(lvalueID(1)))-1 lvalue(1)];
            LFirstpeak(l,:) = [(L_TO(i)+ltpeakid(lvalueID(2)))-1 lvalue(2)];
            l = l+1;
        elseif ltpeakid(lvalueID(2))>ltpeakid(lvalueID(1)) %higher peak first
            [Lmtc(l) LmtcID_nonadj(l)] =
min(LToe((L_TO(i)+ltpeakid(lvalueID(1))):(L_TO(i)+ltpeakid(lvalueID(2)))),3));
            LmtcID(l) = LmtcID_nonadj(l) + (L_TO(i)+ltpeakid(lvalueID(1)))-1;
            LSecondpeak(l,:) = [(L_TO(i)+ltpeakid(lvalueID(2)))-1 lvalue(2)];
            LFirstpeak(l,:) = [(L_TO(i)+ltpeakid(lvalueID(1)))-1 lvalue(1)];
            l = l+1;
        end
    elseif length(lvalueID)==1
        LTMax(lm,:) = [L_TO(i)+ltpeakid-1 ltpeak];
        lm=lm+1;
    end
end

end

r=1;
rm=1;
RTMax=[0 0];
if R_HS(1)<R_TO(1)
    R_HS = R_HS(2:end);
end

if R_TO(end)>R_HS(end)
    R_TO = R_TO(1:end-1);
end

for i=1:length(R_TO)
    [rtpeak rtpeakid] = findpeaks(RToe(R_TO(i):R_HS(i)+5,3),'MinPeakDistance',5);

```

```

[rvalue rvalueID] = sort(rtpeak, 'descend');
if length(rvalueID)>1
    if rtpeakid(rvalueID(2))<rtpeakid(rvalueID(1)) %low peak first
        [Rmtc(r) RmtcID_nonadj(r)] =
min(RToe((R_TO(i)+rtpeakid(rvalueID(2))):(R_TO(i)+rtpeakid(rvalueID(1))),3));
        RmtcID(r) = RmtcID_nonadj(r) + (R_TO(i)+rtpeakid(rvalueID(2)))-1;
        RSecondpeak(r,:) = [(R_TO(i)+rtpeakid(rvalueID(1)))-1 rvalue(1)];
        RFirstpeak(r,:) = [(R_TO(i)+rtpeakid(rvalueID(2)))-1 rvalue(2)];
        r = r+1;
    elseif rtpeakid(rvalueID(2))>rtpeakid(rvalueID(1)) %higher peak first
        [Rmtc(r) RmtcID_nonadj(r)] =
min(RToe((R_TO(i)+rtpeakid(rvalueID(1))):(R_TO(i)+rtpeakid(rvalueID(2))),3));
        RmtcID(r) = RmtcID_nonadj(r) + (R_TO(i)+rtpeakid(rvalueID(1)))-1;
        RSecondpeak(r,:) = [(R_TO(i)+rtpeakid(rvalueID(2)))-1 rvalue(2)];
        RFirstpeak(r,:) = [(R_TO(i)+rtpeakid(rvalueID(1)))-1 rvalue(1)];
        r = r+1;
    end
elseif length(rvalueID)==1
    RTMax(rm,:) = [R_TO(i)+rtpeakid-1 rtpeak];
    rm=rm+1;
end
end

%% Ankle Crossings to find mid swing locations. MTC are defined as the height
%% of the toe at MTC minus the height of the toe at midstance

b = (COM(:,1) > RAnkle(:,1)); % 1--true 0--false
c = (COM(:,1) > LAnkle(:,1)); % 1--true 0--false

xb = diff(b); % +1 => minima indexes (but one)
xc = diff(c); % +1 => minima indexes (but one)

R_AX_temp = find(xb == -1) + 1;
L_AX_temp = find(xc == -1) + 1;

R_AX = R_AX_temp(find(R_AX_temp>R_HS(1) & R_AX_temp<R_TO(end)));
L_AX = L_AX_temp(find(L_AX_temp>L_HS(1) & L_AX_temp<L_TO(end)));

R_Zero = mean(RToe(R_AX,3));
L_Zero = mean(LToe(L_AX,3));
LFirst = LmtcID(1)<RmtcID(1); % 1- left first, 0- right first

%% Plot toe trajectories, mid stance locations, and MTC
% mkdir(['S:\coa\hpl\alex\mos\results\' ftype],file(subject,:))
savefigurefolder = ['S:\coa\hpl\alex\Thesis Analysis\MTC\' group '\ char(file{subject,:})];

LTMIN = min(LToe(:,3))-10;
LTMAX = max(LToe(:,3))+10;
RTMIN = min(RToe(:,3))-10;
RTMAX = max(RToe(:,3))+10;

figure(1);
subplot(2,1,1)

```

```

plot(t_mk,LToe(:,3),'k');
title(['Left Foot' file(subject,:)])
xlabel('AP')
ylabel('Verticle Axis')
axis([0 60 LTMIN LTMAX])
hold on
plot(t_mk(LmtcID),LToe(LmtcID,3),'b*');
hold on
for i=1:length(LmtcID)
    text(t_mk(LmtcID(i))+0.2,LToe(LmtcID(i),3)+30,num2str(i),'FontSize',5);
    hold on
end
plot(t_mk(LFirstpeak(:,1)),LFirstpeak(:,2),'r*')
hold on
plot(t_mk(LSecondpeak(:,1)),LSecondpeak(:,2),'g*')
hold on
plot(t_mk(L_AX),LToe(L_AX,3),'k o')
hold on
plot(t_mk,mean(LToe(L_AX,3))*ones(length(t_mk),1),'r')
hold on
if length(LTMax)>2
    plot(t_mk(LTMax(:,1)),LTMax(:,2),'c*')
end
hold on

```

```

subplot(2,1,2)
plot(t_mk,RToe(:,3),'k');
title('Right Foot')
xlabel('time (s)')
ylabel('Verticle Axis')
axis([0 60 RTMIN RTMAX])
hold on
plot(t_mk(RmtcID),RToe(RmtcID,3),'b*');
hold on
for i=1:length(RmtcID)
    text(t_mk(RmtcID(i)),RToe(RmtcID(i),3)+30,num2str(i),'FontSize',5);
    hold on
end
plot(t_mk(RFirstpeak(:,1)),RFirstpeak(:,2),'r*')
hold on
plot(t_mk(RSecondpeak(:,1)),RSecondpeak(:,2),'g*')
hold on
plot(t_mk(R_AX),RToe(R_AX,3),'k o')
hold on
plot(t_mk,mean(RToe(R_AX,3))*ones(length(t_mk),1),'r')
hold on
if length(RTMax)>2
    plot(t_mk(RTMax(:,1)),RTMax(:,2),'c*')
end
hold on
set(gcf,'units','normalized','outerposition',[0 0 1 1])

```

```

figurename = [savefigurefolder '_0_60.jpg'];
saveas(1,figurename)

```

```

figure(2);
subplot(2,1,1)
plot(t_mk,LToe(:,3),'k');
title(['Left Foot' file(subject,:)])
xlabel('time (s)')
ylabel('Verticle Axis')
axis([60 120 LTMIN LTMAX])
hold on
plot(t_mk(LmtcID),LToe(LmtcID,3),'b*');
hold on
for i=1:length(LmtcID)
    text(t_mk(LmtcID(i))+0.2,LToe(LmtcID(i),3)+30,num2str(i),'FontSize',5);
    hold on
end
plot(t_mk(LFirstpeak(:,1)),LFirstpeak(:,2),'r*')
hold on
plot(t_mk(LSecondpeak(:,1)),LSecondpeak(:,2),'g*')
hold on
plot(t_mk(L_AX),LToe(L_AX,3),'k o')
hold on
plot(t_mk,mean(LToe(L_AX,3))*ones(length(t_mk),1),'r')
hold on
if length(LTMax)>2
    plot(t_mk(LTMax(:,1)),LTMax(:,2),'c*')
end
hold on

subplot(2,1,2)
plot(t_mk,RToe(:,3),'k');
title('Right Foot')
xlabel('time (s)')
ylabel('Verticle Axis')
axis([60 120 RTMIN RTMAX])
hold on
plot(t_mk(RmtcID),RToe(RmtcID,3),'b*');
hold on
for i=1:length(RmtcID)
    text(t_mk(RmtcID(i)),RToe(RmtcID(i),3)+30,num2str(i),'FontSize',5);
    hold on
end
plot(t_mk(RFirstpeak(:,1)),RFirstpeak(:,2),'r*')
hold on
plot(t_mk(RSecondpeak(:,1)),RSecondpeak(:,2),'g*')
hold on
plot(t_mk(R_AX),RToe(R_AX,3),'k o')
hold on
plot(t_mk,mean(RToe(R_AX,3))*ones(length(t_mk),1),'r')
hold on
if length(RTMax)>2
    plot(t_mk(RTMax(:,1)),RTMax(:,2),'c*')
end
hold on
set(gcf,'units','normalized','outerposition',[0 0 1 1])

figurename = [savefigurefolder '_60_120.jpg'];

```

```

saveas(2,figurename)

figure(3);
subplot(2,1,1)
plot(t_mk,LToe(:,3),'k');
title(['Left Foot' file(subject,:)])
xlabel('time (s)')
ylabel('Verticle Axis')
axis([120 180 LTMIN LTMAX])
hold on
plot(t_mk(LmtcID),LToe(LmtcID,3),'b*');
hold on
for i=1:length(LmtcID)
    text(t_mk(LmtcID(i))+0.2,LToe(LmtcID(i),3)+30,num2str(i),'FontSize',5);
    hold on
end
plot(t_mk(LFirstpeak(:,1)),LFirstpeak(:,2),'r*')
hold on
plot(t_mk(LSecondpeak(:,1)),LSecondpeak(:,2),'g*')
hold on
plot(t_mk(L_AX),LToe(L_AX,3),'k o')
hold on
plot(t_mk,mean(LToe(L_AX,3))*ones(length(t_mk),1),'r')
hold on
if length(LTMax)>2
    plot(t_mk(LTMax(:,1)),LTMax(:,2),'c*')
end
hold on

subplot(2,1,2)
plot(t_mk,RToe(:,3),'k');
title('Right Foot')
xlabel('time (s)')
ylabel('Verticle Axis')
axis([120 180 RTMIN RTMAX])
hold on
plot(t_mk(RmtcID),RToe(RmtcID,3),'b*');
hold on
for i=1:length(RmtcID)
    text(t_mk(RmtcID(i)),RToe(RmtcID(i),3)+30,num2str(i),'FontSize',5);
    hold on
end
plot(t_mk(RFirstpeak(:,1)),RFirstpeak(:,2),'r*')
hold on
plot(t_mk(RSecondpeak(:,1)),RSecondpeak(:,2),'g*')
hold on
plot(t_mk(R_AX),RToe(R_AX,3),'k o')
hold on
plot(t_mk,mean(RToe(R_AX,3))*ones(length(t_mk),1),'r')
hold on
if length(RTMax)>2
    plot(t_mk(RTMax(:,1)),RTMax(:,2),'c*')
end
hold on
set(gcf,'units','normalized','outerposition',[0 0 1 1])

```



```

figurename = [savefigurefolder '_120_180.jpg'];
saveas(3,figurename)

if keepgraphs == 0
close all
end
%%

fname = ['S:\coa\hpl\alex\Thesis Analysis\MTC\' group '_results.xlsx'];

outleft = [(1:length(Lmtc))' (Lmtc-L_Zero)' (LFirstpeak(:,2)-L_Zero) (LSecondpeak(:,2)-L_Zero)];

outright = [(1:length(Rmtc))' (Rmtc-R_Zero)' (RFirstpeak(:,2)-R_Zero) (RSecondpeak(:,2)-R_Zero)];

xlswrite(fname,outleft,char(file{ subject,:}),['A3']);
pause(1)
if length(LTMax)>2
xlswrite(fname,(LTMax(:,2)-L_Zero),char(file{ subject,:}),['E3']);
end
pause(1)

xlswrite(fname,outright,char(file{ subject,:}),['F3']);
pause(1)
if length(RTMax)>2
xlswrite(fname,(RTMax(:,2)-R_Zero),char(file{ subject,:}),['J3']);
end
pause(1)

xlswrite(fname,[R_Zero;L_Zero;LFirst],char(file{ subject,:}),['L3']);

end

```

Code used to process accelerometry data to calculate RMS and frequency content:

```

clear;
keepgraphs = 0; %0-no, 1-yes
filtneeded = 1;

% group = ['controls'];
% file =
{'MSC03';'MSC04';'MSC05';'MSC11';'MSC13';'MSC14';'MSC15';'MSC17';'MSC18';'MSC21';'MSC24';'MSC26';'M
SC29';'MSC31';'MSC32';'MSC34';'MSC35';'MSC37';'MSC38';'MSC40';'MSC42';'MSC43';'MSC47';'MSC48';'MSC4
9';'MSC50';'MSC51'};

% group = ['nonfallers'];
% file =
{'MS05';'MS09';'MS13';'MS16';'MS17';'MS18';'MS23';'MS26';'MS29';'MS31';'MS32';'MS44';'MS45';'MS47';'MS48';
'MS49';'MS50';'MS60';'MS69';'MS71';'MS78';'MS81';'MS82';'MS84';'MS85';'MS89';'MS105';'MS112'};

% group = ['fallers'];
% file =
{'MS12';'MS14';'MS21';'MS30';'MS33';'MS36';'MS37';'MS56';'MS57';'MS59';'MS61';'MS66';'MS67';'MS76';'MS91';
'MS95';'MS97';'MS100';'MS108';'MS109';'MS110';'MS111';'MS113';'MS119';'MS121';'MS122';'MS124'};

```

```

group = ['controls_rep'];
file = {'MSC07';'MSC09';'MSC19';'MSC20';'MSC30'};

%% Linear measures from trunk accelerometry: RMS and Frequency Dispersion

title = {'subject' 'AP_rms' 'ML_rms' 'VT_rms' 'AP_25' 'AP_75' 'ML_25' 'ML_75' 'VT_25' 'VT_75'};
xlswrite(['S:\coa\hpl\alex\thesis analysis\Trunk_Linear\Linear results.xlsx'],title,group,['A1']);

for subject = 1:length(file);
clearvars -except file group subject

if length(group) == 12
data = importdata(['S:\coa\motion_analysis_data\MS study\Controls\' char(file{subject,:}) '\Mobility Lab SYNC\'
char(file{subject,:}) 'C5_t1.csv']);
else
data = importdata(['S:\coa\motion_analysis_data\MS study\MS subjects\' char(file{subject,:}) '\Mobility Lab
SYNC\' char(file{subject,:}) 'C5_t1.csv']);
end
% Determine the order of the opal sensors in the CSV file

temp_str = data.textdata{4,1};
temp_ind = find(temp_str == ':');

opal1_name = temp_str(temp_ind(1)+1:temp_ind(2)-1);
opal2_name = temp_str(temp_ind(2)+1:temp_ind(3)-1);
opal3_name = temp_str(temp_ind(3)+1:temp_ind(4)-1);
opal4_name = temp_str(temp_ind(4)+1:temp_ind(5)-1);
opal5_name = temp_str(temp_ind(5)+1:temp_ind(6)-1);
opal6_name = temp_str(temp_ind(6)+1:end);

clear temp_str
clear temp_ind

% Load acceleration values

temp_str = data.textdata(1,:);
temp_ind = strfind(temp_str,'Acceleration X (m/s^2)');

j = 0;

temp_col = zeros(1,6);

for i = 1:length(temp_ind)
    if temp_ind{i} == 1
        j = j + 1;
        temp_col(j) = i-1;
    end
end

if strcmp(opal1_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(1));

```

```

    trunk_acc_y_unf = data.data(:,temp_col(1)+1);
    trunk_acc_z_unf = data.data(:,temp_col(1)+2);
elseif strcmp(opal2_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(2));
    trunk_acc_y_unf = data.data(:,temp_col(2)+1);
    trunk_acc_z_unf = data.data(:,temp_col(2)+2);
elseif strcmp(opal3_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(3));
    trunk_acc_y_unf = data.data(:,temp_col(3)+1);
    trunk_acc_z_unf = data.data(:,temp_col(3)+2);
elseif strcmp(opal4_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(4));
    trunk_acc_y_unf = data.data(:,temp_col(4)+1);
    trunk_acc_z_unf = data.data(:,temp_col(4)+2);
elseif strcmp(opal5_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(5));
    trunk_acc_y_unf = data.data(:,temp_col(5)+1);
    trunk_acc_z_unf = data.data(:,temp_col(5)+2);
elseif strcmp(opal6_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(6));
    trunk_acc_y_unf = data.data(:,temp_col(6)+1);
    trunk_acc_z_unf = data.data(:,temp_col(6)+2);
end

clear temp_col

% Subtract the mean value in order to offset effect of gravity

trunk_acc_x_norm = trunk_acc_x_unf - mean(trunk_acc_x_unf);
trunk_acc_y_norm = trunk_acc_y_unf - mean(trunk_acc_y_unf);
trunk_acc_z_norm = trunk_acc_z_unf - mean(trunk_acc_z_unf);

% Low pass 4th order Butterworth filter at 20 Hz

Fs = 128;

f_c = 20;

[b,a] = butter(4,2*(f_c/Fs),'low');

AP = filter(b,a,trunk_acc_z_norm);
ML = filter(b,a,trunk_acc_y_norm);
VT = filter(b,a,trunk_acc_x_norm);

AP_rms = rms(AP);
ML_rms = rms(ML);
VT_rms = rms(VT);

%% Power Frequencies
% figure(2)

Y = fft(AP);
N = length(Y);
Y(1) = [];
power = abs(Y(1:round(N/2))).^2;

```

```

nyquist = Fs/2;
freq = (1:round(N/2))/(round(N/2))*nyquist;
% subplot(3,1,1)
% plot(freq,power)
% title('Power Spectrum AP')

totalPower = sum(power);
AP_25 = freq(find(cumsum(power)>(.25*totalPower),1));
AP_75 = freq(find(cumsum(power)>(.75*totalPower),1));

clear Y N power freq

Y = fft(ML);
N = length(Y);
Y(1) = [];
power = abs(Y(1:round(N/2))).^2;
nyquist = Fs/2;
freq = (1:round(N/2))/(round(N/2))*nyquist;
% subplot(3,1,2)
% plot(freq,power)
% title('Power Spectrum ML')

totalPower = sum(power);
ML_25 = freq(find(cumsum(power)>(.25*totalPower),1));
ML_75 = freq(find(cumsum(power)>(.75*totalPower),1));

clear Y N power freq

Y = fft(VT);
N = length(Y);
Y(1) = [];
power = abs(Y(1:round(N/2))).^2;
nyquist = Fs/2;
freq = (1:round(N/2))/(round(N/2))*nyquist;
% subplot(3,1,3)
% plot(freq,power)
% title('Power Spectrum VT')

totalPower = sum(power);
VT_25 = freq(find(cumsum(power)>(.25*totalPower),1));
VT_75 = freq(find(cumsum(power)>(.75*totalPower),1));

out = {char(file{subject,:}) AP_rms ML_rms VT_rms AP_25 AP_75 ML_25 ML_75 VT_25 VT_75};

xlswrite(['S:\coa\hpl\alex\thesis analysis\Trunk_Linear\Linear results.xlsx'],out,group,['A' num2str(subject+1)]);
end

```

**Code used to process accelerometry data to calculate find the embedding dimension and time delay for each subject:**

```
clear;

% group = ['controls'];
% file =
{'MSC03';'MSC04';'MSC11';'MSC13';'MSC14';'MSC15';'MSC17';'MSC18';'MSC21';'MSC24';'MSC26';'MSC29';'M
SC31';'MSC32';'MSC34';'MSC35';'MSC37';'MSC38';'MSC40';'MSC42';'MSC43';'MSC47';'MSC48';'MSC49';'MSC5
0';'MSC51'};

% group = ['nonfallers'];
% file =
{'MS05';'MS09';'MS13';'MS16';'MS17';'MS18';'MS23';'MS26';'MS29';'MS31';'MS32';'MS44';'MS45';'MS47';'MS48';
'MS49';'MS50';'MS60';'MS69';'MS71';'MS78';'MS81';'MS82';'MS84';'MS85';'MS89';'MS105';'MS112'};

% group = ['fallers'];
% file =
{'MS12';'MS14';'MS21';'MS30';'MS33';'MS36';'MS37';'MS56';'MS57';'MS59';'MS61';'MS66';'MS67';'MS76';'MS91';
'MS95';'MS97';'MS100';'MS108';'MS109';'MS110';'MS111';'MS113';'MS119';'MS121';'MS122';'MS124'};

title = {'subject' 'ST_mean' 'AP_dim_cut' 'ML_dim_cut' 'VT_dim_cut' 'AP_tau_cut' 'ML_tau_cut' 'VT_tau_cut'
'AP_dim_res' 'ML_dim_res' 'VT_dim_res' 'AP_tau_res' 'ML_tau_res' 'VT_tau_res'};
xlswrite(['S:\coa\hpl\alex\thesis analysis\Trunk_Nonlinear\dim_tau_all.xlsx'],title,group,['A1']);

for subject = 1:2%length(file);
clearvars -except file group subject

if length(group) == 8
data = importdata(['S:\coa\motion_analysis_data\MS study\Controls\' char(file{subject,:}) '\Mobility Lab SYNC\'
char(file{subject,:}) 'C5_t1.csv']);
else
data = importdata(['S:\coa\motion_analysis_data\MS study\MS subjects\' char(file{subject,:}) '\Mobility Lab
SYNC\' char(file{subject,:}) 'C5_t1.csv']);
end

Fs = 128;

% Determine the order of the opal sensors in the CSV file

temp_str = data.textdata{4,1};
temp_ind = find(temp_str == ':');

opal1_name = temp_str(temp_ind(1)+1:temp_ind(2)-1);
opal2_name = temp_str(temp_ind(2)+1:temp_ind(3)-1);
opal3_name = temp_str(temp_ind(3)+1:temp_ind(4)-1);
opal4_name = temp_str(temp_ind(4)+1:temp_ind(5)-1);
opal5_name = temp_str(temp_ind(5)+1:temp_ind(6)-1);
opal6_name = temp_str(temp_ind(6)+1:end);

clear temp_str
clear temp_ind
```

```

% Load acceleration values

temp_str = data.textdata(1,:);
temp_ind = strfind(temp_str,'Acceleration X (m/s^2)');

j = 0;

temp_col = zeros(1,6);

for i = 1:length(temp_ind)
    if temp_ind{i} == 1
        j = j + 1;
        temp_col(j) = i-1;
    end
end

if strcmp(opal1_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(1));
    trunk_acc_y_unf = data.data(:,temp_col(1)+1);
    trunk_acc_z_unf = data.data(:,temp_col(1)+2);
elseif strcmp(opal2_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(2));
    trunk_acc_y_unf = data.data(:,temp_col(2)+1);
    trunk_acc_z_unf = data.data(:,temp_col(2)+2);
elseif strcmp(opal3_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(3));
    trunk_acc_y_unf = data.data(:,temp_col(3)+1);
    trunk_acc_z_unf = data.data(:,temp_col(3)+2);
elseif strcmp(opal4_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(4));
    trunk_acc_y_unf = data.data(:,temp_col(4)+1);
    trunk_acc_z_unf = data.data(:,temp_col(4)+2);
elseif strcmp(opal5_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(5));
    trunk_acc_y_unf = data.data(:,temp_col(5)+1);
    trunk_acc_z_unf = data.data(:,temp_col(5)+2);
elseif strcmp(opal6_name,'Trunk') == 1
    trunk_acc_x_unf = data.data(:,temp_col(6));
    trunk_acc_y_unf = data.data(:,temp_col(6)+1);
    trunk_acc_z_unf = data.data(:,temp_col(6)+2);
end

trunk_AP = trunk_acc_z_unf - mean(trunk_acc_z_unf);
trunk_ML = trunk_acc_y_unf - mean(trunk_acc_y_unf);
trunk_VT = trunk_acc_x_unf - mean(trunk_acc_x_unf);

%%
% subplot(3,1,1)
% plot(trunk_AP)
% subplot(3,1,2)
% plot(trunk_ML)
% subplot(3,1,3)
% plot(trunk_VT)
%%

```

```

temp_str = data.textdata(1,:);%read all headers
temp_ind = strfind(temp_str,'Angular Velocity Y (rad/s)');%is a 1 for every

j = 0;

temp_col = zeros(1,6);

for i = 1:length(temp_ind)
    if temp_ind{i} == 1
        j = j + 1;
        temp_col(j) = i-1;
    end
end

% if strcmp(opal1_name,'Right Leg') == 1
%     r_leg_ang_vel_ml = data.data(:,temp_col(1));
% elseif strcmp(opal2_name,'Right Leg') == 1
%     r_leg_ang_vel_ml = data.data(:,temp_col(2));
% elseif strcmp(opal3_name,'Right Leg') == 1
%     r_leg_ang_vel_ml = data.data(:,temp_col(3));
% elseif strcmp(opal4_name,'Right Leg') == 1
%     r_leg_ang_vel_ml = data.data(:,temp_col(4));
% elseif strcmp(opal5_name,'Right Leg') == 1
%     r_leg_ang_vel_ml = data.data(:,temp_col(5));
% elseif strcmp(opal6_name,'Right Leg') == 1
%     r_leg_ang_vel_ml = data.data(:,temp_col(6));
% end

if strcmp(opal1_name,'Left Leg') == 1
    r_leg_ang_vel_ml = data.data(:,temp_col(1));
elseif strcmp(opal2_name,'Left Leg') == 1
    r_leg_ang_vel_ml = data.data(:,temp_col(2));
elseif strcmp(opal3_name,'Left Leg') == 1
    r_leg_ang_vel_ml = data.data(:,temp_col(3));
elseif strcmp(opal4_name,'Left Leg') == 1
    r_leg_ang_vel_ml = data.data(:,temp_col(4));
elseif strcmp(opal5_name,'Left Leg') == 1
    r_leg_ang_vel_ml = data.data(:,temp_col(5));
elseif strcmp(opal6_name,'Left Leg') == 1
    r_leg_ang_vel_ml = data.data(:,temp_col(6));
end

clear temp_col

%%
[~,r_leg_midswing_locs] = findpeaks(-r_leg_ang_vel_ml,'MINPEAKHEIGHT',max(-
r_leg_ang_vel_ml*.5),'MINPEAKDISTANCE',50);

t = [0:1/Fs:length(r_leg_ang_vel_ml)/Fs-1/Fs];

figure(1)
plot(t,r_leg_ang_vel_ml,t(r_leg_midswing_locs),r_leg_ang_vel_ml(r_leg_midswing_locs),'r*')

```

```

figurename = ['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group \' char(file{subject,:}) 'midswing.fig'];
saveas(1,figurename)
clear figurename

%%

n = round((length(r_leg_midswing_locs)-60)/2);

Trunk_AP_cut = resample(trunk_AP(r_leg_midswing_locs(n):r_leg_midswing_locs(n+60)),60,Fs);
Trunk_ML_cut = resample(trunk_ML(r_leg_midswing_locs(n):r_leg_midswing_locs(n+60)),60,Fs);
Trunk_VT_cut = resample(trunk_VT(r_leg_midswing_locs(n):r_leg_midswing_locs(n+60)),60,Fs);
t_cut = resample([0:1/Fs:length(Trunk_AP_cut)/Fs-1/Fs],60,Fs);

ST_mean = t_cut(end)/60;

Trunk_AP_res = resample(Trunk_AP_cut,6000,length(Trunk_AP_cut));
Trunk_ML_res = resample(Trunk_ML_cut,6000,length(Trunk_ML_cut));
Trunk_VT_res = resample(Trunk_VT_cut,6000,length(Trunk_VT_cut));
F_res = 6000/t_cut(end);
t_res = [0:1/F_res:length(Trunk_AP_res)/F_res-1/F_res];

save(['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group \' char(file{subject,:})
'Trunk_AP_cut.dat'],Trunk_AP_cut','-ascii');
save(['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group \' char(file{subject,:})
'Trunk_ML_cut.dat'],Trunk_ML_cut','-ascii');
save(['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group \' char(file{subject,:})
'Trunk_VT_cut.dat'],Trunk_VT_cut','-ascii');

save(['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group \' char(file{subject,:})
'Trunk_AP_res.dat'],Trunk_AP_res','-ascii');
save(['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group \' char(file{subject,:})
'Trunk_ML_res.dat'],Trunk_ML_res','-ascii');
save(['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group \' char(file{subject,:})
'Trunk_VT_res.dat'],Trunk_VT_res','-ascii');

figure(2)
subplot(2,1,1)
plot(t_cut,Trunk_AP_cut,'r',t_res,Trunk_AP_res,'b')
legend('original','resampled')
title('Trunk AP')
xlabel('time (sec)')
ylabel('acc (g)')
axis([0 20 min(Trunk_AP_cut)-3 max(Trunk_AP_cut)+3])
subplot(2,1,2)
plot(t_cut,Trunk_AP_cut,'r',t_res,Trunk_AP_res,'b')
xlabel('time (sec)')
ylabel('acc (g)')
axis([0 5 min(Trunk_AP_cut)-3 max(Trunk_AP_cut)+3])

figurename = ['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group \' char(file{subject,:})
'comp_sample_freq.fig'];
saveas(2,figurename)
clear figurename
%% AP

```



```

% cut

data = Trunk_AP_cut;
% Parameters
L=32; % max window size for AMI
MaxDim=14; %max window size for embedding dimension
Rtol=15; Atol=2; % Threshold to determine the FNN

[tau,v_AMI]=AMI(data, L); % Find the time lag - tau
fprintf('Tau = %d\r',tau);
[FN,dim] = FNN(data,tau,MaxDim, Rtol,Atol ); % Find the embedding dimension
fprintf('Embedding dimension = %d\r',dim);
% Plot the data
figure(3)
% Plot of False Nearest Neighbors vs Embedding dimension
subplot(2,1,1)
AMI_plot(tau,v_AMI,L )
xlabel('Time lag')
subplot(2,1,2)
% Plot of False Nearest Neighbours vs Embedding Dimension
plot(FN,'o');
axis([1 MaxDim 0 1]);
xlabel('Dimension','FontWeight','bold');
ylabel('% FN','FontWeight','bold');
set(gca,'YTickLabel',[0;10;20;30;40;50;60;70;80;90;100])
axis([1 MaxDim 0 1]);
title(strcat('% False Nearest Neighbors; dim = ', int2str(dim)));
hold on
scatter(dim,FN(dim),'r')
set(gcf, 'Position', [100 100 500 400])
hold off

AP_tau_cut = tau;
AP_dim_cut = dim;

figurename = ['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group '\ char(file{subject,:})
'_AP_dim_tau_cut.jpeg'];
saveas(3,figurename)

% res
%%
data = Trunk_AP_res;
% Parameters
L=32; % max window size for AMI
MaxDim=14; %max window size for embedding dimension
Rtol=15; Atol=2; % Threshold to determine the FNN

[tau,v_AMI]=AMI(data, L); % Find the time lag - tau
fprintf('Tau = %d\r',tau);
[FN,dim] = FNN(data,tau,MaxDim, Rtol,Atol ); % Find the embedding dimension
fprintf('Embedding dimension = %d\r',dim);
% Plot the data
figure(4)
% Plot of False Nearest Neighbors vs Embedding dimension
subplot(2,1,1)

```

```

AMI_plot(tau,v_AMI,L )
xlabel('Time lag')
subplot(2,1,2)
% Plot of False Nearest Neighbours vs Embedding Dimension
plot(FN,'o:');
axis([1 MaxDim 0 1]);
xlabel('Dimension','FontWeight','bold');
ylabel('% FN','FontWeight','bold');
set(gca,'YTickLabel',[0;10;20;30;40;50;60;70;80;90;100])
axis([1 MaxDim 0 1]);
title(strcat('% False Nearest Neighbors; dim = ', int2str(dim)));
hold on
scatter(dim,FN(dim),'r')
set(gcf, 'Position', [100 100 500 400])
hold off

AP_tau_res = tau;
AP_dim_res = dim;

figurename = ['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group '\ char(file{subject,:})
'_AP_dim_tau_res.jpeg'];
saveas(4,figurename)

%% ML

% cut

data = Trunk_ML_cut;
% Parameters
L=32; % max window size for AMI
MaxDim=14; %max window size for embedding dimension
Rtol=15; Atol=2; % Threshold to determine the FNN

[tau,v_AMI]=AMI(data, L); % Find the time lag - tau
fprintf('Tau = %d\r',tau);
[FN,dim] = FNN(data,tau,MaxDim, Rtol,Atol ); % Find the embedding dimension
fprintf('Embedding dimension = %d\r',dim);
% Plot the data
figure(5)
% Plot of False Nearest Neighbors vs Embedding dimension
subplot(2,1,1)
AMI_plot(tau,v_AMI,L )
xlabel('Time lag')
subplot(2,1,2)
% Plot of False Nearest Neighbours vs Embedding Dimension
plot(FN,'o:');
axis([1 MaxDim 0 1]);
xlabel('Dimension','FontWeight','bold');
ylabel('% FN','FontWeight','bold');
set(gca,'YTickLabel',[0;10;20;30;40;50;60;70;80;90;100])
axis([1 MaxDim 0 1]);
title(strcat('% False Nearest Neighbors; dim = ', int2str(dim)));
hold on
scatter(dim,FN(dim),'r')
set(gcf, 'Position', [100 100 500 400])

```

```

hold off

ML_tau_cut = tau;
ML_dim_cut = dim;

figurename = ['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group '\' char(file{subject,:})
'_ML_dim_tau_cut.jpeg'];
saveas(5,figurename)

%% res
%

data = Trunk_ML_res;
% Parameters
L=32; % max window size for AMI
MaxDim=14; %max window size for embedding dimension
Rtol=15; Atol=2; % Threshold to determine the FNN

[tau,v_AMI]=AMI(data, L); % Find the time lag - tau
fprintf('Tau = %d\r',tau);
[FN,dim] = FNN(data,tau,MaxDim, Rtol,Atol ); % Find the embedding dimension
fprintf('Embedding dimension = %d\r',dim);
% Plot the data
figure(6)
% Plot of False Nearest Neighbors vs Embedding dimension
subplot(2,1,1)
AMI_plot(tau,v_AMI,L )
xlabel('Time lag')
subplot(2,1,2)
% Plot of False Nearest Neighbours vs Embedding Dimension
plot(FN,'o:');
axis([1 MaxDim 0 1]);
xlabel('Dimension','FontWeight','bold');
ylabel('% FN','FontWeight','bold');
set(gca,'YTickLabel',[0;10;20;30;40;50;60;70;80;90;100])
axis([1 MaxDim 0 1]);
title(strcat('% False Nearest Neighbors; dim = ', int2str(dim)));
hold on
scatter(dim,FN(dim),'r')
set(gcf, 'Position', [100 100 500 400])
hold off

ML_tau_res = tau;
ML_dim_res = dim;

figurename = ['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group '\' char(file{subject,:})
'_ML_dim_tau_res.jpeg'];
saveas(6,figurename)

% VT

% cut
data = Trunk_VT_cut;
% Parameters
L=32; % max window size for AMI
MaxDim=14; %max window size for embedding dimension

```

```

Rtol=15; Atol=2; % Threshold to determine the FNN

[tau,v_AMI]=AMI(data, L); % Find the time lag - tau
fprintf('Tau = %d\r',tau);
[FN,dim] = FNN(data,tau,MaxDim, Rtol,Atol ); % Find the embedding dimension
fprintf('Embedding dimension = %d\r',dim);
% Plot the data
figure(7)
% Plot of False Nearest Neighbors vs Embedding dimension
subplot(2,1,1)
AMI_plot(tau,v_AMI,L )
xlabel('Time lag')
subplot(2,1,2)
% Plot of False Nearest Neighbours vs Embedding Dimension
plot(FN,'o:');
axis([1 MaxDim 0 1]);
xlabel('Dimension','FontWeight','bold');
ylabel('% FN','FontWeight','bold');
set(gca,'YTickLabel',[0;10;20;30;40;50;60;70;80;90;100])
axis([1 MaxDim 0 1]);
title(strcat('% False Nearest Neighbors; dim = ', int2str(dim)));
hold on
scatter(dim,FN(dim),'r')
set(gcf, 'Position', [100 100 500 400])
hold off

VT_tau_cut = tau;
VT_dim_cut = dim;

figurename = ['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group '\' char(file{subject,:})
'_VT_dim_tau_cut.jpeg'];
saveas(7,figurename)

% res

data = Trunk_VT_res;
% Parameters
L=32; % max window size for AMI
MaxDim=14; %max window size for embedding dimension
Rtol=15; Atol=2; % Threshold to determine the FNN

[tau,v_AMI]=AMI(data, L); % Find the time lag - tau
fprintf('Tau = %d\r',tau);
[FN,dim] = FNN(data,tau,MaxDim, Rtol,Atol ); % Find the embedding dimension
fprintf('Embedding dimension = %d\r',dim);
% Plot the data
figure(8)
% Plot of False Nearest Neighbors vs Embedding dimension
subplot(2,1,1)
AMI_plot(tau,v_AMI,L )
xlabel('Time lag')
subplot(2,1,2)
% Plot of False Nearest Neighbours vs Embedding Dimension
plot(FN,'o:');
axis([1 MaxDim 0 1]);
xlabel('Dimension','FontWeight','bold');

```

```

ylabel('% FN','FontWeight','bold');
set(gca,'YTickLabel',[0;10;20;30;40;50;60;70;80;90;100])
axis([1 MaxDim 0 1]);
title(strcat('% False Nearest Neighbors; dim = ',int2str(dim)));
hold on
scatter(dim,FN(dim),'r')
set(gcf,'Position',[100 100 500 400])
hold off

VT_tau_res = tau;
VT_dim_res = dim;

figurename = ['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\' group '\' char(file{subject,:})
'_VT_dim_tau_res.jpeg'];
saveas(8,figurename)

%%
% AP_dim_res=[];
% AP_tau_res=[];
out = {char(file{subject,:}) ST_mean AP_dim_cut ML_dim_cut VT_dim_cut AP_tau_cut ML_tau_cut VT_tau_cut
AP_dim_res ML_dim_res VT_dim_res AP_tau_res ML_tau_res VT_tau_res};

xlswrite(['S:\coa\hpl\alex\thesis analysis\Trunk_nonlinear\dim_tau_all.xlsx'],out,group,['A' num2str(subject+1)]);

close all
end

function [tau,v_AMI]=AMI(data, L)

%L = 32; %maximal lag -- arbitrarily selected, must be much smaller than length(data)

N=length(data);
bins=128; %number of bins used for histogram calculation
%bins=floor(1+log2(N-L)+0.5);

epsilon = eps; %or use epsilon = 1e-10;

data = data - min(data); % making all the data points positive
data = 1 + floor(data/(max(data)/(bins-epsilon))); %scaling the data
v=zeros(L,1); %create a zero vector
overlap=N+1-L;
increment= 1/overlap;
one = ones(overlap,1); %create a column vector with all elements being one

% MUTUAL INFORMATION
% I (time_lag) = sum [ p(x(t), x(t + time_lag))*log[(p(x(t),p(x + time_lag))/p(x(t))*p(x(t+time_lag)))]

%find probability p(x(t))= pA
pA = sparse (data(1:overlap),one,increment);
%e.g. when overlap = N+1-L = 6001+1-32= 5970, max(data(1:overlap))=129,
%creaing a histogram with (129-1) bins
% sum(pA)= 1 --> 100 % in total

for lag = 0: L -1
    %find probablity p(x(t+time_lag))=pB, sum(pB)=1

```

```

pB = sparse(one, data(1+lag:overlap+lag), increment);
%find joining probability p(A,B)=p(x(t),x(t+time_lag))
pAB = sparse(data(1:overlap),data(1+lag:overlap+lag),increment);
[A, B, AB]=find(pAB);
v(lag+1)=sum(AB.*log2(AB./(pA(A).*pB(B')))); %Average Mutual Information
end

v_AMI=v;
%Take time_lag when 1st min(I(time_lag))occurs for values of time_lag near
%this minimum, the coordinate system produced by time delay vector is
%essentially as good as that of the time_lag whih is the actual 1st min(I(time_lag))
for i = 1: length(v)-1
    if (find((v(i)<v(i+1))&&(v(i)<v(i-1)))) == 1
        x(i)=i;
    end
end

A = sparse(x);
A= find(A);
tau = A(1); % tau = 1st min(I(time_lag))

function [FN,dim] = FNN(data,tau,MaxDim, Rtol,Atol )
%
% % Determine the embedding dimension for a time series using the false
% nearest neighbors
% References: "Determining embedding dimension for phase-space reconstruction using
% a geometrical construction", M. B. Kennel, R. Brown, and H.D.I. Abarbanel,
% Physical Review A, Vol 45, No 6, 15 March 1992, pp 3403-3411.
% Inputs:
% data: a time series
% tau: time delay
% MaxDim: maximum embedding dimension
% Rtol: threshold for the first criterion
% Atol: threshold for teh second criterion
% PerFFNs: Threshold for percentage false nearest neighbors

n=length(data)-tau*MaxDim; % # of data points to be used
RA=std(data); %the nominal "radius" of the attractor

data=data';
z = data(1:n);
y = [];
FN = [];

global yq m_search L_done pqd pqr pqz b_upper b_lower sort_list node_list

m_search = 2; % just search for the nearest point; the closest will be yq
% itself and the next its neighbor

indx=[1:n];

for dim = 1:MaxDim
    y = [y; z];
    z = data(1+tau*dim:n+tau*dim);
    L = zeros(1,n);

```

```

%fprintf('Partitioning data for dim = %d\n',dim)
kd_part(y, z, 512); % put the data into 512-point bins <-- this needs optimization
%fprintf('Checking for false nearest neighbors\n')

for i = 1:length(indx)

    yq = y(:,indx(i)); % set up the next point to check

    % set up the bounds, which start at +/- infinity
    b_upper = Inf*ones(size(yq));
    b_lower = -b_upper;

    % and set up storage for the results
    pqd = Inf*ones(1,m_search);
    pqr = [];
    pqz = [];
    L_done = 0;

    kdsearch(1); % start searching at the root (node 1)

    distance = pqz(1) - pqz(2);
    if abs(distance) > pqd(2)*Rtol L(i) = 1; end
    if sqrt(pqd(2)^2+distance^2)/RA > Atol L(i) = 1; end

end % i loop

FN = [FN sum(L)/n];

end % d loop

dE=FN(:,1:length(FN))';

%%%%%%%%%%%%%%

for i = 2:13
    if (dE(i)==0)||((dE(i-1)>dE(i)&&(dE(i)< dE(i+1))))
        dim(i)= i;
        i=i+1;
    else
        i=i+1;
    end
end
%%%%%%%%%%%%%%

dim=[];
for i = 1: 13
    %if dE(i)-dE(i+1)<=0
    if dE(i)-dE(i+1)<=0.001
        dim(i) = i;
    end
end

A=sparse(dim);
A=find(A);
dim=A(1);

```

```

function [FN,dim] = FNN(data,tau,MaxDim, Rtol,Atol )
%
% % Determine the embedding dimension for a time series using the false
% nearest neighbors
% References: "Determining embedding dimension for phase-space reconstruction using
% a geometrical construction", M. B. Kennel, R. Brown, and H.D.I. Abarbanel,
% Physical Review A, Vol 45, No 6, 15 March 1992, pp 3403-3411.
% Inputs:
% data: a time series
% tau: time delay
% MaxDim: maximum embedding dimension
% Rtol: threshold for the first criterion
% Atol: threshold for the second criterion
% PerFFNs: Threshold for percentage false nearest neighbors

n=length(data)-tau*MaxDim; % # of data points to be used
RA=std(data); %the nominal "radius" of the attractor

data=data';
z = data(1:n);
y = [];
FN = [];

global yq m_search L_done pqd pqr pqz b_upper b_lower sort_list node_list

m_search = 2; % just search for the nearest point; the closest will be yq
% itself and the next its neighbor

indx=[1:n];

for dim = 1:MaxDim
    y = [y; z];
    z = data(1+tau*dim:n+tau*dim);
    L = zeros(1,n);
    %fprintf('Partitioning data for dim = %d\n',dim)
    kd_part(y, z, 512); % put the data into 512-point bins <-- this needs optimization
    %fprintf('Checking for false nearest neighbors\n')

    for i = 1:length(indx)

        yq = y(:,indx(i)); % set up the next point to check

        % set up the bounds, which start at +/- infinity
        b_upper = Inf*ones(size(yq));
        b_lower = -b_upper;

        % and set up storage for the results
        pqd = Inf*ones(1,m_search);
        pqr = [];
        pqz = [];
        L_done = 0;

        kdsearch(1); % start searching at the root (node 1)

        distance = pqz(1) - pqz(2);
        if abs(distance) > pqd(2)*Rtol L(i) = 1; end
    end
end

```



```

        if sqrt(pqd(2)^2+distance^2)/RA > Atol L(i) = 1; end

    end % i loop

    FN = [FN sum(L)/n];

end % d loop

dE=FN(:,1:length(FN))';

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

for i = 2:13
    if (dE(i)==0)||((dE(i-1)>dE(i)&&(dE(i)< dE(i+1))))
        dim(i)= i;
        i=i+1;
    else
        i=i+1;
    end
end
%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%

dim=[];
for i = 1: 13
    %if dE(i)-dE(i+1)<=0
    if dE(i)-dE(i+1)<=0.001
        dim(i) = i;
    end
end

A=sparse(dim);
A=find(A);
dim=A(1);

function [] = kd_part(y_in, z_in, bin_size);
% Create a kd-tree and partitioned database for
% efficiently finding the nearest neighbors to a point
% in a d-dimensional space.
% Usage: [] = kd_part(y_in, z_in, bin_size);
%
% y_in: original phase space data
% z_in: original phase space data corresponding to y_in
% bin_size: maximum number of distinct points for each bin
% The outputs are placed into global variables used by
% kdsearch and its subroutines.

% The outputs are...
% sort_list(:,1): discriminator: dimension to use in dividing data
% sort_list(:,2): partition: boundary for dividing data
% node_list(i,:): contains data for the i-th partition
% node_list(:,1): 1st element in y of this partition
% node_list(:,2): last element in y of this partition
% node_list(:,3): location in node_list of left branch
% node_list(:,4): location in node_list of right branch
% y_model: phase space data partitioned into a binary tree

```

```

% z_model: phase space data corresponding to each y_model point

% Algorithms from:
%
% "Data Structures for Range Searching", J.L. Bentley, J.H. Friedman,
% ACM Computing Surveys, Vol 11, No 4, p 397-409, December 1979
%
% "An Algorithm for Finding Best Matches in Logarithmic Expected Time",
% J.H. Friedman, J.L. Bentley, R.A. Finkel, ACM Transactions on
% Mathematical Software, Vol 3, No 3, p 209-226, September 1977.

global y_model z_model sort_list node_list

y_model = y_in;
z_model = z_in;
[d, n_y] = size(y_model);
% d: dimension of phase space
% n_y: number of points to put into partitioned database

% Set up first node...
node_list = [1 n_y 0 0];
sort_list = [0 0];

% ...and the information about the number of nodes so far
node = 1;
last = 1;

while node <= last % check if the node can be divided

range = [];
segment = node_list(node,1):node_list(node,2);
for i = 1:d range = [range max(y_model(i,segment))-min(y_model(i,segment))]; end
if max(range) > 0 & length(segment) >= bin_size % it is divisible
[r_sort, index] = sort(range);
yt = y_model(:,segment);
zt = z_model(:,segment);
[y_sort, y_index] = sort(yt(index(d,:),:));
% estimate where the cut should go
[junk, tlen] = size(yt);
if rem(tlen,2) % yt has an odd number of elements
cut = y_sort((tlen+1)/2);
else % yt has an even number of elements
cut = (y_sort(tlen/2)+y_sort(tlen/2+1))/2;
end % of the median calculation
L = y_sort <= cut;
if sum(L) == tlen % then the right node will be empty...
L = y_sort < cut; % ...so use a slightly different boundary
cut = (cut+max(y_sort(L)))/2;
end % of the cut adjustment
% adjust the order of the data
y_model(:,segment) = yt(:,y_index);
z_model(:,segment) = zt(:,y_index);
% mark this as a non-terminal node
sort_list(node,:) = [index(d) cut];
node_list(node,3) = last + 1;
node_list(node,4) = last + 2;

```

```

last = last + 2;
% add the information for the new nodes
node_list = [node_list; segment(1) segment(1)+sum(L)-1 0 0];
node_list = [node_list; segment(1)+sum(L) segment(tlen) 0 0];
sort_list = [sort_list; 0 0; 0 0]; % assume they're terminal for the moment
end % of the splitting process

node = node + 1;

end % of the while loop

function [] = kdsearch(node)
% Search a kd_tree to find the nearest matches to the global variable
% yq, a vector. The nearest matches will be put in the global variable
% pqr, and their distances in pqd. See loclin_kd for a usage example.

global y_model z_model yq m_search L_done pqd pqr pqz b_upper b_lower sort_list node_list

if L_done return, end

if node_list(node,3) == 0 % it's a terminal node, so...
    % first, compute the distances...
    yi = node_list(node,1:2); % index bounds of all y_model to consider
    yt = y_model(:,yi(1):yi(2));
    zt = z_model(:,yi(1):yi(2));
    dist = zeros(size(yt(1,:))); % initialize
    d = length(yq); % get the dimension
    for j = 1:d,
        dist = dist + (yt(j,:)-yq(j)).^2;
    end
    dist = sqrt(dist);
    % and then sort them and load pqd, pqr, and pqz
    pqd = [dist pqd]; % distances ^2
    pqr = [yt pqr]; % current nearest neighbors
    pqz = [zt pqz]; % corresponding entries in z
    [pqd, index] = sort(pqd); % distances
    [junk, len] = size(pqz);
    if length(index) > len
        pqr = pqr(:,index(1:length(pqz)));
        pqz = pqz(:,index(1:length(pqz)));
    else
        pqr = pqr(:,index);
        pqz = pqz(:,index);
    end % if statement
    % keep only the first m_search points
    if length(pqd) > m_search, pqd = pqd(1:m_search); end
    [junk, len] = size(pqz);
    if len > m_search
        pqr = pqr(:,1:m_search);
        pqz = pqz(:,1:m_search);
    end % if statement
    if within
        L_done = 1;
    end % if statement
    return
else % it's not a terminal node, so search a little deeper

```

```

disc = sort_list(node,1);
part = sort_list(node,2);
if yq(disc) <= part % determine which child node to go to
    temp = b_upper(disc);
    b_upper(disc) = part;
    kdsearch(node_list(node,3))
    b_upper(disc) = temp;
else
    temp = b_lower(disc);
    b_lower(disc) = part;
    kdsearch(node_list(node,4))
    b_lower(disc) = temp;
end % of the if statement
if L_done return, end
if yq(disc) <= part % determin whether other child node needs to be searched
    temp = b_lower(disc);
    b_lower(disc) = part;
    if overlap
        kdsearch(node_list(node,4));
    end
    b_lower(disc) = temp;
else
    temp = b_upper(disc);
    b_upper(disc) = part;
    if overlap
        kdsearch(node_list(node,3));
    end
    b_upper(disc) = temp;
end % if statement
if L_done return, end
end % of the outermost if

```

```

function [x,y] = embed(z,v,w)

```

```

% [x,y] or x= embed(z,lags) or embed(z,dim,lag)
% embed z using given lags or dim and lag
% embed(z,dim,lag) == embed(z,[0:lag:lag*(dim-1)])
% negative entries of lags are into future
%
% If return is [x,y], then x is the positive lags and y the negative lags
% Order of rows in x and y the same as sort(lags)
%
% defaults:
% dim = 3
% lag = 1
% lags = [0 1 2]; or [-1 lags] when two outputs and no negative lags

```

```

% Copyright (c) 1994 by Kevin Judd.
% Please see the copyright notice included in this distribution
% for full details.
%
% NAME embed.m
% $Id$

```

```

if nargin==3
    v= 0:w:w*(v-1);
end;
if nargin==1
    v= [0 1 2];
end
if nargout==2 & min(v)>=0
    v= [-1 v];
end
lags= sort(v);

dim = length(lags);

[c,n] = size(z);
if c ~= 1
    z = z';
    [c,n] = size(z);
end
if c ~= 1
    error('Embed needs a vector as first arg. ');
end

if n < lags(dim)
    error('Vector is too small to be embedded with the given lags');
end

w = lags(dim) - lags(1);    % window
m = n - w;                % Rows of x
t = (1:m) + lags(dim);     % embed times

x = zeros(dim,m);

for i=1:dim
    x(i,:) = z( t - lags(i) );
end

if nargout==2
    id= find(v<0);
    y= x(id,:);
    id= find(v>=0);
    x= x(id,:);
end;

function L = within

% algorithms from:
% "Data Structures for Range Searching", J.L. Bentley, J.H. Friedman,
% ACM Computing Surveys, Vol 11, No 4, p 397-409, December 1979
%
% "An Algorithm for Finding Best Matches in Logarithmic Expected Time",
% J.H. Friedman, J.L. Bentley, R.A. Finkel, ACM Transactions on
% Mathematical Software, Vol 3, No 3, p 209-226, September 1977.

global y_model z_model yq m_search L_done pqd pqr pqz b_upper b_lower sort_list node_list

```

```

dist = pqd(m_search);

for i = 1:length(yq)

if abs(yq(i)-b_lower(i))<=dist | abs(yq(i)-b_upper(i))<=dist
    L = 0;
    return
end % of the if statement

end % of the i loop

L = 1;

return

function L = overlap

% algorithms from:
% "Data Structures for Range Searching", J.L. Bentley, J.H. Friedman,
% ACM Computing Surveys, Vol 11, No 4, p 397-409, December 1979
%
% "An Algorithm for Finding Best Matches in Logarithmic Expected Time",
% J.H. Friedman, J.L. Bentley, R.A. Finkel, ACM Transactions on
% Mathematical Software, Vol 3, No 3, p 209-226, September 1977.

global y_model z_model yq m_search L_done pqr pqz b_upper b_lower sort_list node_list

dist = pqd(m_search)^2;
sum = 0;

for i = 1:length(yq)

if yq(i) < b_lower(i)
    sum = sum + (yq(i)-b_lower(i))^2;
    if sum > dist
        L = 0;
        return
    end % of the sum > dist if
elseif yq(i) > b_upper(i)
    sum = sum + (yq(i)-b_upper(i))^2;
    if sum > dist
        L = 0;
        return
    end % of the sum > dist if
end % of the yq(i) <> a bound if

end % of the i loop

L = 1;
return

```

### Code used to calculate Lyapunov exponents:

```
clear

axis = {'AP';'ML';'VT'};
dim = 7;
tau = [8;9;6];

% file =
{'MSC03';'MSC04';'MSC11';'MSC13';'MSC14';'MSC15';'MSC17';'MSC18';'MSC21';'MSC24';'MSC26';'MSC29';'MSC31';
'MSC32';'MSC34';'MSC35';'MSC37';'MSC38';'MSC40';'MSC42';'MSC43';'MSC47';'MSC48';'MSC49';'MSC50';'MSC51';.
..
%
'MS05';'MS09';'MS13';'MS16';'MS17';'MS18';'MS23';'MS26';'MS29';'MS31';'MS32';'MS44';'MS45';'MS47';'MS48';'M
S49';'MS50';'MS60';'MS69';'MS71';'MS78';'MS81';'MS82';'MS84';'MS85';'MS89';'MS105';'MS112';...
%
'MS12';'MS14';'MS21';'MS30';'MS33';'MS36';'MS37';'MS56';'MS57';'MS59';'MS61';'MS66';'MS67';'MS76';'MS91';'M
S95';'MS97';'MS100';'MS108';'MS109';'MS110';'MS111';'MS113';'MS119';'MS121';'MS122';'MS124'};

file = {'MSC07';'MSC09';'MSC20'};

% ject = 60; %
for sub = 1:length(file)

for dir = 1:3
data = importdata(['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\dat_files\' char(file{sub,:}) 'Trunk_'
char(axis{dir,:}) '_down.dat']);

[LyE,SUM_all]=Lyapunov(data,dim,tau(dir));
LYEEE(sub,dir)=LyE;

end
sub
end

function [LyE,SUM_all]=Lyapunov(X,dim,tau)

% dim: embedding dimension
% tau: time lag
% DT: time between data samples required only for normalization of the
%     exponent
% A: relative accuracy of the data below which noise is expected to
%     dominate
% SCALMX: length scale on which the local structure of attractor is no
%         longer being probe
% n: number of sample intervals over which each pair of points is followed
%     before a new pair is chosen. If n is too large teh trajectories get too
%     far apart and the exponential divergence of the orbit is lost.
% IND: initial points to fiducial trajectory

%change paramters here

DT=1;
```

```

A= 10^(-4);
SCALMX=(max(X)-min(X))/10;
n=3;
IND=1;

[LyE,SUM_all]=LyE_Wolf(X,dim,tau,DT,A,SCALMX,n,IND);
function [ZLAP,SUM_all]=LyE_Wolf(X,dim,tau,DT, SCALMN, SCALMX, EVOLV,IND)

[r c]=size(X);
if c > r
    X=X';
end

SUM=0.0; % Sum holds running exponent estimate sans 1/time;
count=1;
ITS=0; % total number of propagation steps

NPT=length(X)-dim*tau-EVOLV; %Calculate useful size of data

%Find nearest neighbor to first data point
DI=1.e38;

%Dont take point too close to fiducial point

for i=1:NPT
    %Compute separation between fiducial point and candiate
    D=0;
    for j=1:dim
        D=D+(X(IND+(j-1)*tau)-X(i+(j-1)*tau))^2;
    end
    D=sqrt(D);

    %Store the best point so far but no closer than noise scale
    if (D <= DI) && (D >= SCALMN)
        DI=D;
        IND2=i;
    end
end

while (IND < NPT)
    %get coordinates of evolved points
    PT=GetCoordinate(X,IND,IND2,EVOLV,dim,tau);
    PT1=PT(:,1)';
    PT2=PT(:,2)';

    %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    %Plot
    %SensitiveDependenceIC(X,dim,tau,IND,IND2,EVOLV)

    %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    %compute final separation between pair, update exponent
    DF=0;
    for j=1:dim
        DF=DF+(PT1(j)-PT2(j))^2;
    end
end

```



```

end
DF=sqrt(DF);

ITS=ITS+1;
SUM=SUM+log(DF/DI)/(EVOLV*DT);
SUM_all(count)= log(DF/DI)/(EVOLV*DT);
count=count+1;

ZLAP=SUM/ITS;

%Look for replacement point
%ZMULT is multiplier of SCALMX when go to longer distances
INDOLD=IND2;
ZMULT=1;
ANGLMX=0.3;
THMIN=3.14;

%Search over all points
[DII IND2]=GetNewPt(X, dim, tau, IND, EVOLV, PT1, PT2,SCALMX, ZMULT,
SCALMN,DF,ANGLMX,INDOLD);

IND=IND+EVOLV;
DI=DII;
end
ZLAP;

function [DII, IND2]=GetNewPt(X, dim, tau, IND, EVOLV, PT1, PT2,SCALMX, ZMULT, SCALMN,
DF,ANGLMX,INDOLD)

THMIN=3.14;
NPT=length(X)-dim*tau-EVOLV;
for i=1:NPT
    III=abs(i-(IND+EVOLV));
    if (III >= 10)
        DNEW=0;
        for j=1:dim
            DNEW=DNEW+(PT1(j)-X(i+(j-1)*tau))^2;
        end
        DNEW=sqrt(DNEW);

        %look further away than noise scale, closer than ZMULT*SCALM
        if (DNEW <= ZMULT*SCALMX)&&(DNEW >= SCALMN)
            %Find angular change old to new vector
            DOT= sum((PT1'-X(i+((1:dim)-1)*tau)).*(PT1'-PT2'));
            CTH=abs(DOT/(DNEW*DF));
            if (CTH > 1.0)
                CTH=1.0;
            end
            TH=acos(CTH);
            %Save point with smallest angular change so far
            if (TH <= THMIN)
                THMIN=TH;
            end
            DII=DNEW;
            IND2=i;
        end
    end
end

```

```

        end
    end
end
end

if (THMIN >= ANGLMX)
    [DII, IND2]=LookLongerDistance(X, dim, tau, IND, EVOLV, PT1, PT2,SCALMX, ZMULT, SCALMN,DF,
    ANGLMX,INDOLD);
end

function [x,y] = embed(z,v,w)

% [x,y] or x= embed(z,lags) or embed(z,dim,lag)
% embed z using given lags or dim and lag
% embed(z,dim,lag) == embed(z,[0:lag:lag*(dim-1)])
% negative entries of lags are into future
%
% If return is [x,y], then x is the positive lags and y the negative lags
% Order of rows in x and y the same as sort(lags)
%
% defaults:
% dim = 3
% lag = 1
% lags = [0 1 2]; or [-1 lags] when two outputs and no negative lags

% Copyright (c) 1994 by Kevin Judd.
% Please see the copyright notice included in this distribution
% for full details.
%
% NAME embed.m
% $Id$

if nargin==3
    v= 0:w:w*(v-1);
end;
if nargin==1
    v= [0 1 2];
end
if nargout==2 & min(v)>=0
    v= [-1 v];
end
lags= sort(v);

dim = length(lags);

[c,n] = size(z);
if c ~= 1
    z = z';
    [c,n] = size(z);
end
if c ~= 1
    error('Embed needs a vector as first arg.');
```

```

if n < lags(dim)
    error('Vector is too small to be embedded with the given lags');
end

w = lags(dim) - lags(1);    % window
m = n - w;                % Rows of x
t = (1:m) + lags(dim);     % embed times

x = zeros(dim,m);

for i=1:dim
    x(i,:) = z( t - lags(i) );
end

if nargout==2
    id= find(v<0);
    y= x(id,:);
    id= find(v>=0);
    x= x(id,:);
end;

function PT=GetCoordinate(X,IND,IND2,EVOLV,dim,tau)

if min((length(X)>IND+EVOLV+((1:dim)-1)*tau))&& min((length(X)>IND2+EVOLV+((1:dim)-1)*tau))
    PT1=[X(IND+EVOLV+((1:dim)-1)*tau)'];
    PT2=[X(IND2+EVOLV+((1:dim)-1)*tau)'];
    PT=[PT1' PT2'];
else
    disp('Exceeds the length of X')
end

function [DII, IND2]=LookLongerDistance(X, dim, tau, IND, EVOLV, PT1, PT2,SCALMX, ZMULT,
SCALMN,DF, ANGLMX,INDOLD)

%Can't find a replacement -- look at longer distances
ZMULT = ZMULT+1;
if (ZMULT<5)
    [DII,IND2]=GetNewPt(X, dim, tau, IND, EVOLV, PT1, PT2,SCALMX, ZMULT,
SCALMN,DF,ANGLMX,INDOLD);
    %disp('here1')
else
    % No replacement at 5*SCALE, double search angle, reset distance
    ZMULT=1.0;
    ANGLMX=2*ANGLMX;
    if (ANGLMX < 3.14)
        [DII,IND2]=GetNewPt(X, dim, tau, IND, EVOLV, PT1, PT2,SCALMX, ZMULT,
SCALMN,DF,ANGLMX,INDOLD);
    else
        IND2=INDOLD+EVOLV;
        DII=DF;
    end
end
end

```

### Code used to calculate Sample Entropy:

```
clear

axis = {'AP';'ML';'VT'};

tau = [8;9;6];

% file =
{'MSC03';'MSC04';'MSC11';'MSC13';'MSC14';'MSC15';'MSC17';'MSC18';'MSC21';'MSC24';'MSC26';'MSC29';'M
SC31';'MSC32';'MSC34';'MSC35';'MSC37';'MSC38';'MSC40';'MSC42';'MSC43';'MSC47';'MSC48';'MSC49';'MSC5
0';'MSC51';...
%
'MS05';'MS09';'MS13';'MS16';'MS17';'MS18';'MS23';'MS26';'MS29';'MS31';'MS32';'MS44';'MS45';'MS47';'MS48';
MS49';'MS50';'MS60';'MS69';'MS71';'MS78';'MS81';'MS82';'MS84';'MS85';'MS89';'MS105';'MS112';...
%
'MS12';'MS14';'MS21';'MS30';'MS33';'MS36';'MS37';'MS56';'MS57';'MS59';'MS61';'MS66';'MS67';'MS76';'MS91';
MS95';'MS97';'MS100';'MS108';'MS109';'MS110';'MS111';'MS113';'MS119';'MS121';'MS122';'MS124'};

file = {'MSC07';'MSC09';'MSC19';'MSC20';'MSC30'};

m = 3;
R=0.2;
for sub = 1:length(file)

for dir = 1:3
data = importdata(['S:\coa\hpl\alex\Thesis Analysis\trunk_nonlinear\dat_files\' char(file{sub,:}) 'Trunk_'
char(axis{dir,:}) '_down.dat']);

    SE = SampEntHPL(data, m, R, tau(dir));
    SaEn(sub,dir)=SE;

end
sub
end

function SE = SampEnt(data, m, R, varTau)
% Function to find Sample Entropy using the method described by Richman et
% al. 2000
% J McCamley 7/16/2015

% Define R as r times the standard deviation
r = R * std(data);
u = data;
N = length(u);
tau = varTau;

%Jordan Craig Added time delay sections - fall 2015
for i = 1:N-m*tau
    for j = 1:N-m*tau
        for k = 1:m
            dij(k) = abs(u(i+((k-1)*tau))-u(j+((k-1)*tau)));
        end
        di(j) = max(dij);
    end
end
```

```

end
d = find(di<=r); % find the vectors that are less than "r" distant from one another
nm = length(d)-1; % subtract the self match
Bm(i) = nm/(N-(m*tau)-1);
end
Bmr = sum(Bm)/(N-(m*tau));

for i = 1:N-m*tau
    for j = 1:N-m*tau
        for k = 1:m+1
            dij(k) = abs(u(i+((k-1)*tau))-u(j+((k-1)*tau)));
        end
        di(j) = max(dij);
    end
    d = find(di<=r); % find the vectors that are less than "r" distant from one another
    nm = length(d)-1; % subtract the self match
    Am(i) = nm/(N-(m*tau)-1);
end
Amr = sum(Am)/(N-(m*tau));

B = (((N-(m*tau)-1)*(N-(m*tau)))/2)*Bmr;
A = (((N-(m*tau)-1)*(N-(m*tau)))/2)*Amr;
SE = -log(A/B);
end

```